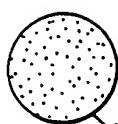


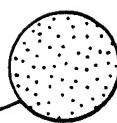
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FIG. 1



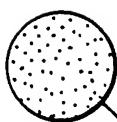
[SEQ. ID NO: 3]

X-C-C-T-T-G-A-G-A-T-T-T-C-C-C-T-C
5' 3'

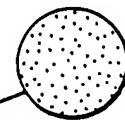


G-G-A-A-C-T-C-T-A-A-A-G-G-G-A-G-X
3' 5'

[SEQ. ID NO: 4]



X-C-C-T-T-G-A-G-A-T-T-T-C-C-C-T-C
G-G-A-A-C-T-C-T-A-A-A-G-G-G-A-G-X



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FIG. 2

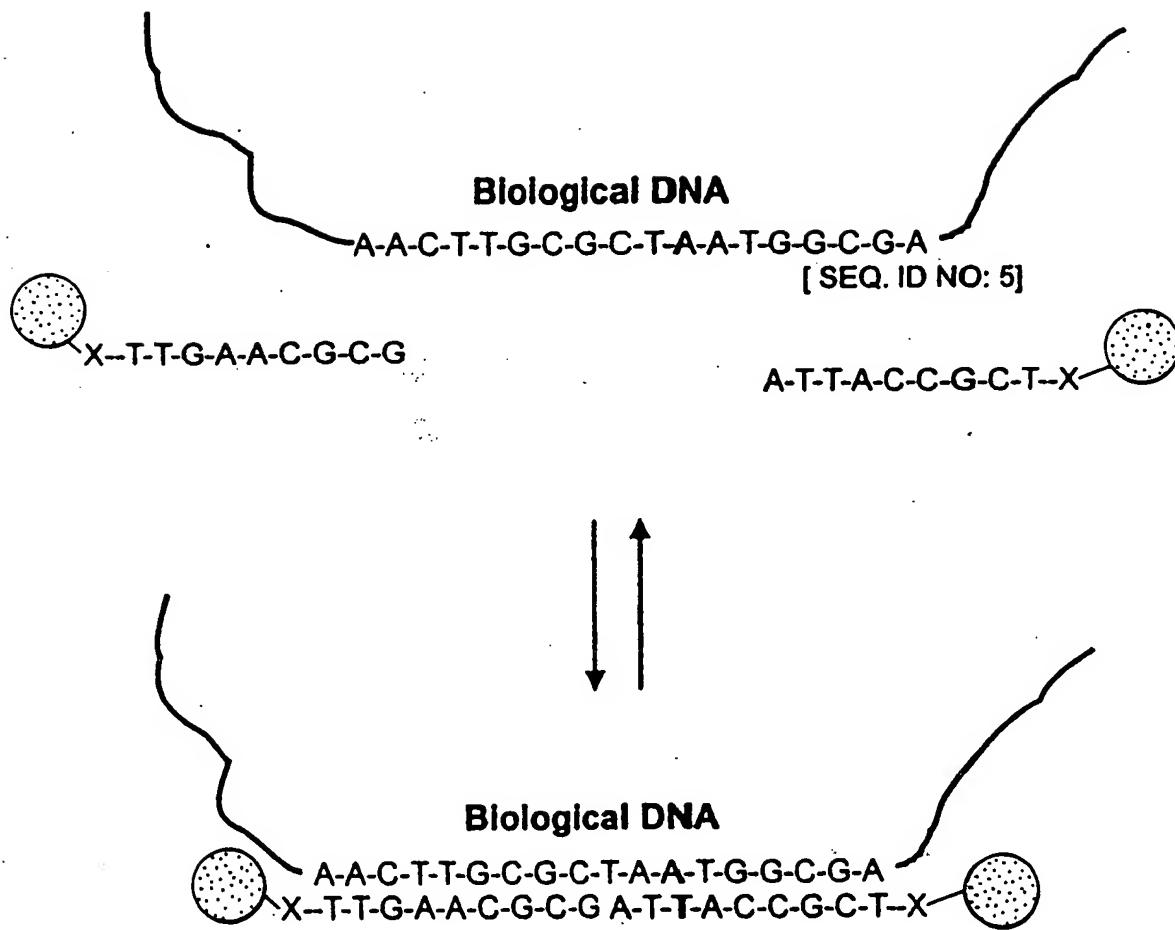


FIG. 3

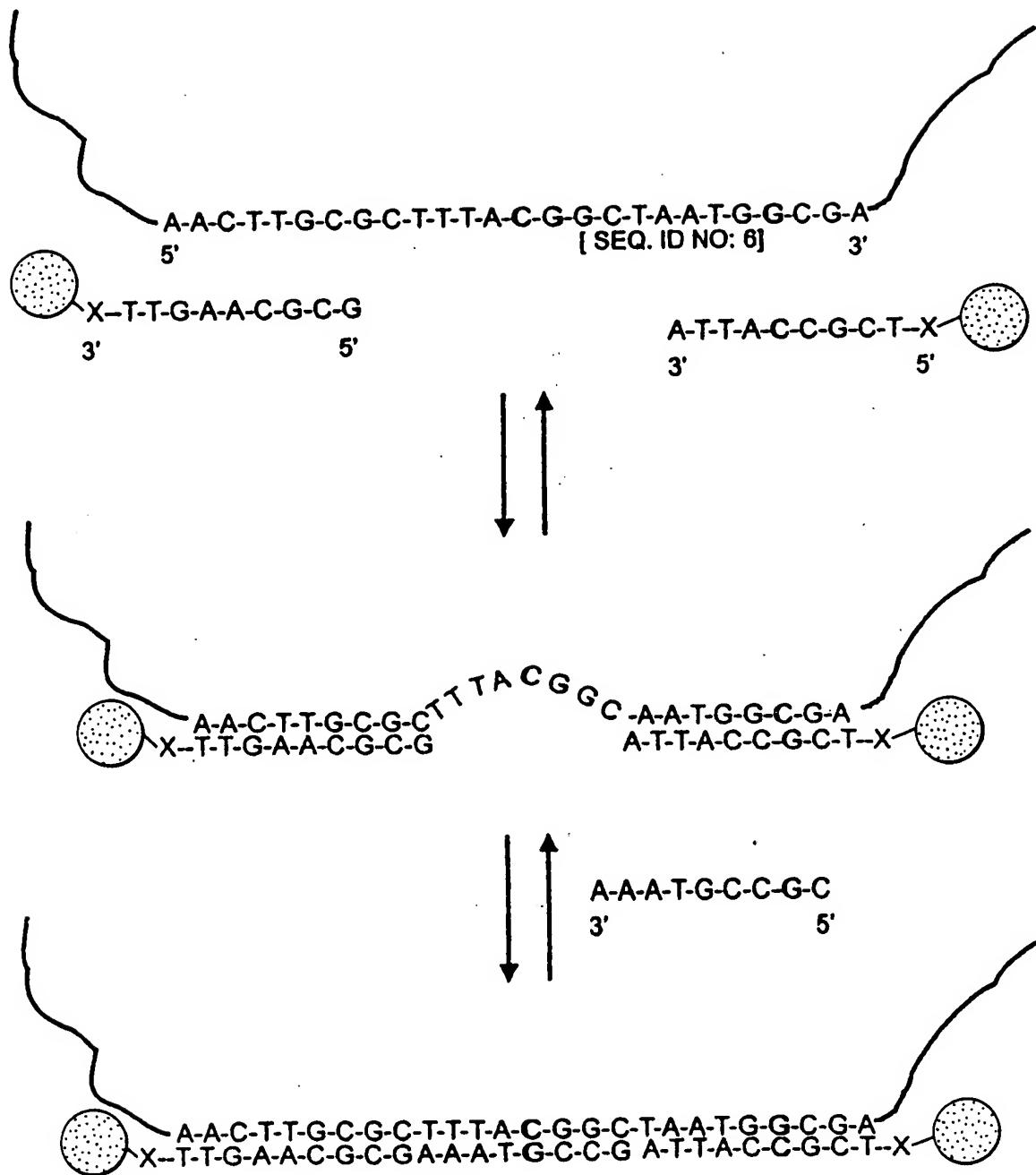


FIG. 4

5' A-T-G-G-C-A-A-C-T-A-T-A-C-G-C-T-A-G
 3' [SEQ. ID NO: 2] →
 5' A-T-A-T-G-C-G-C-G-A-T-C-T-C-A-G-C-A-A-A
 [SEQ. ID NO:1] →

Linking oligonucleotide

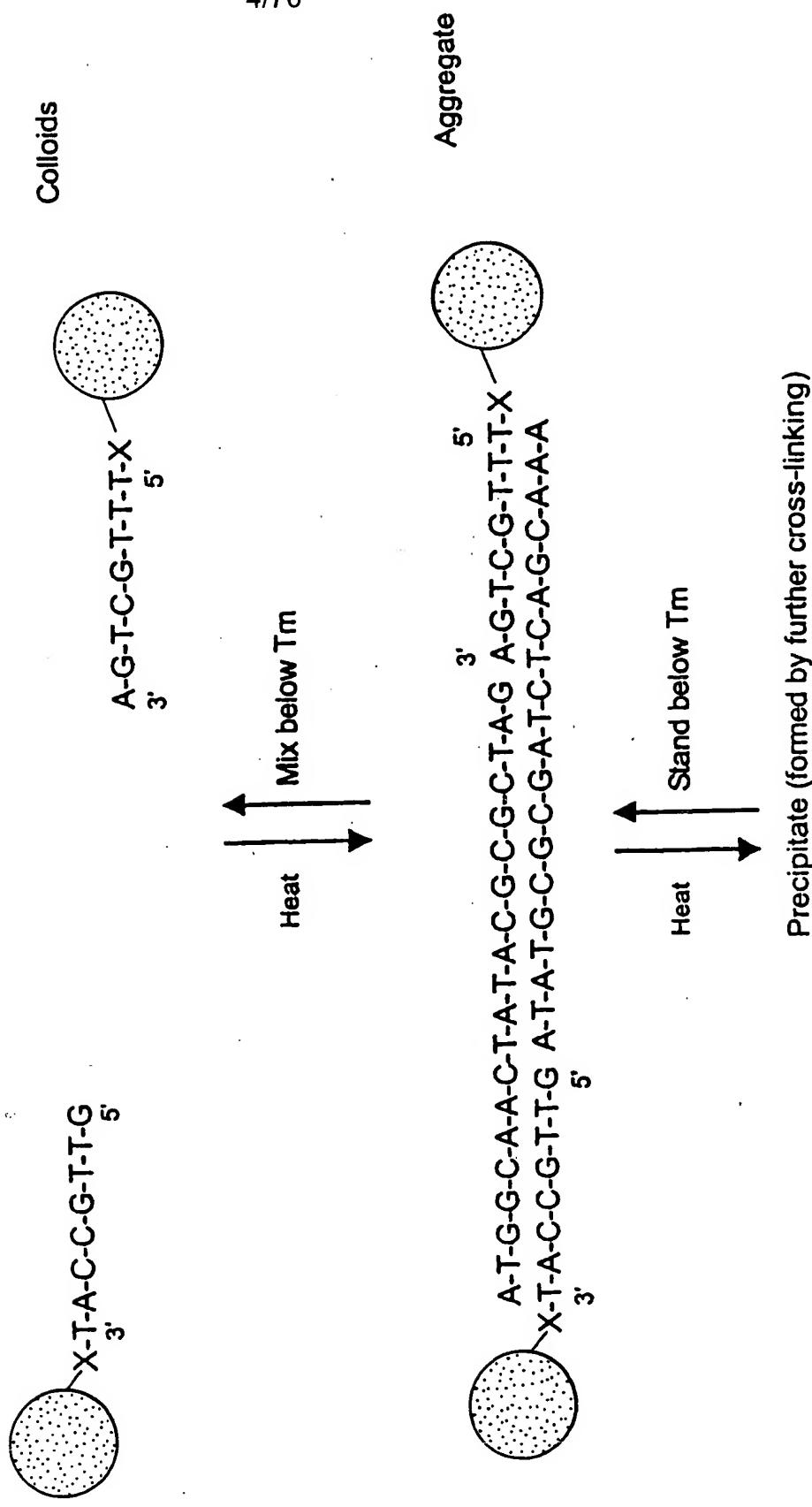
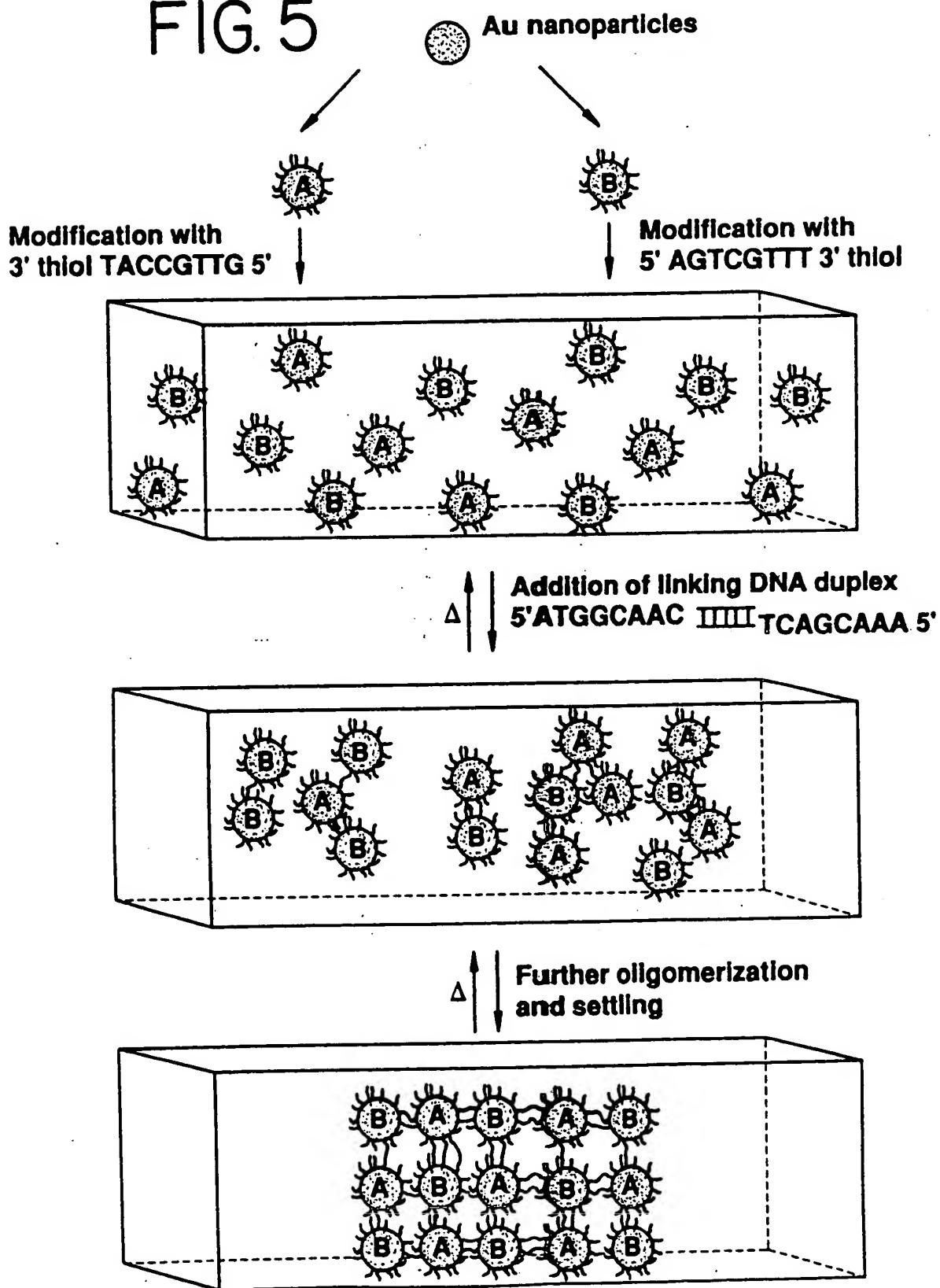


FIG. 5



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FIG. 6A FIG. 6B FIG. 6C

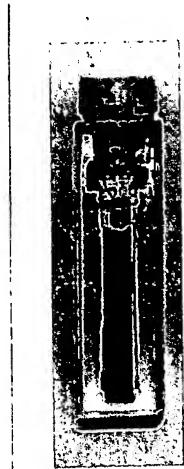


FIG. 7

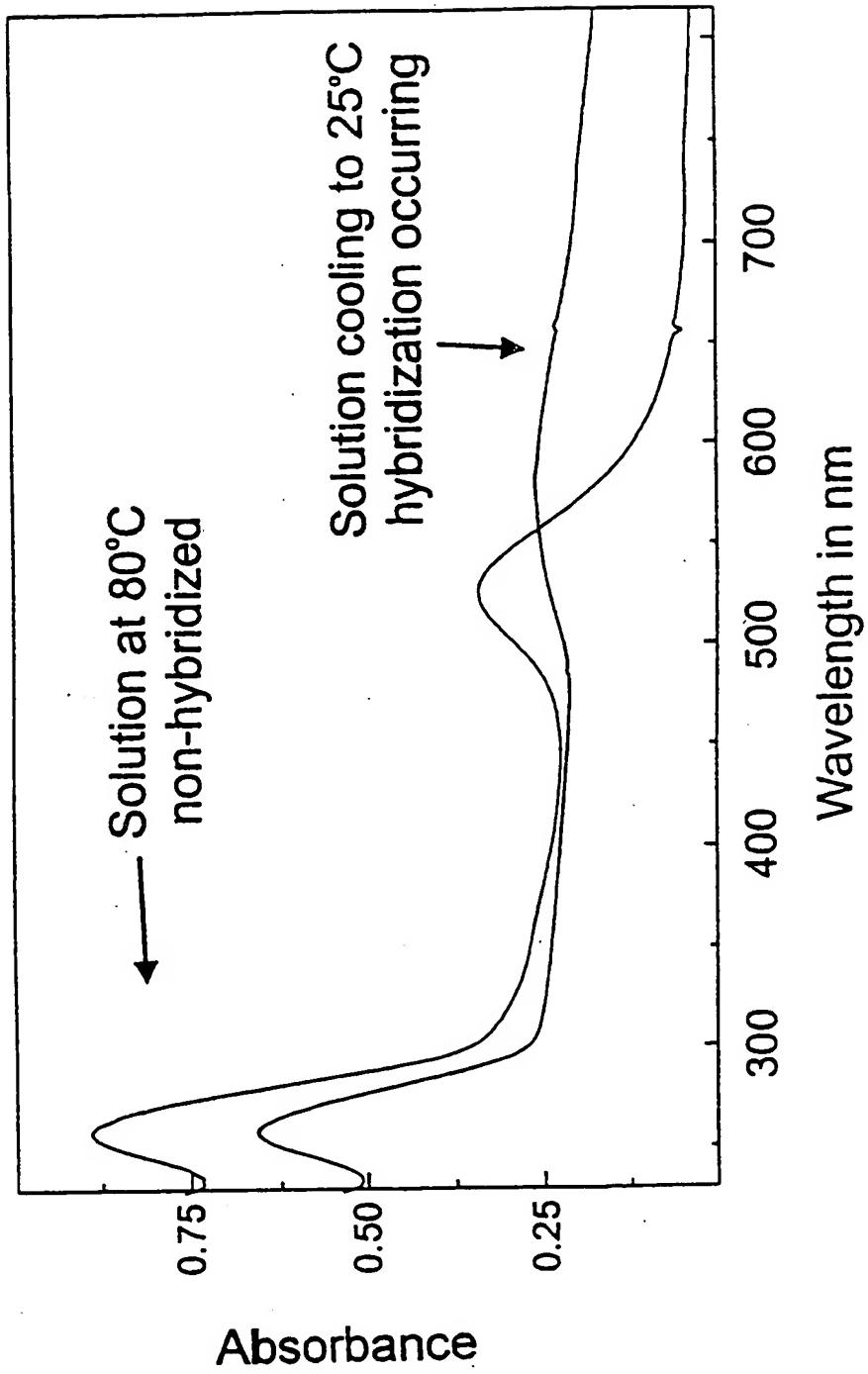


FIG. 8A

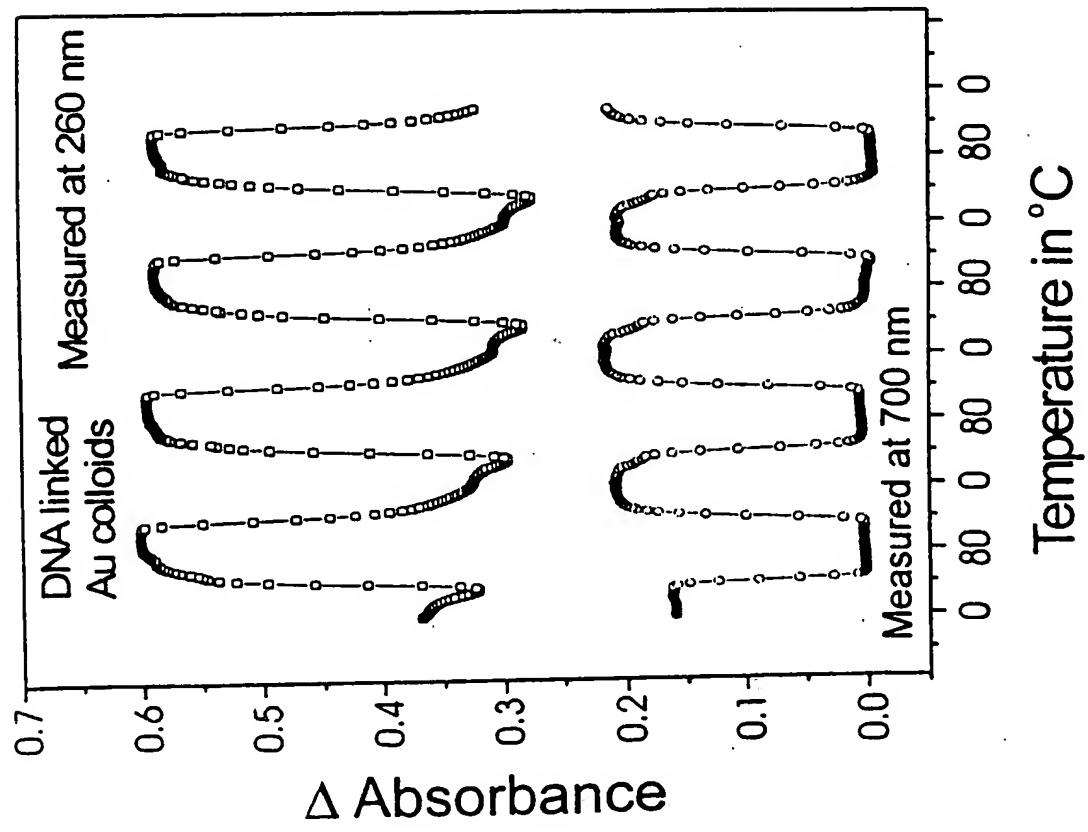
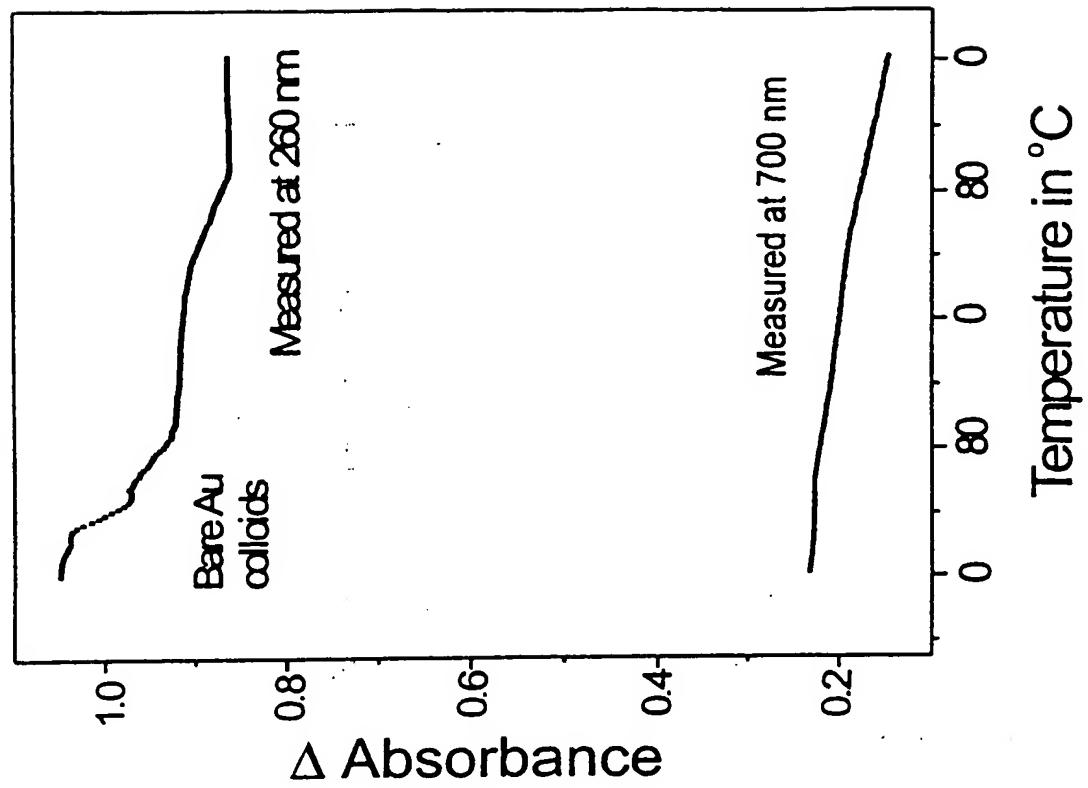


FIG. 8B



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FIG. 9A

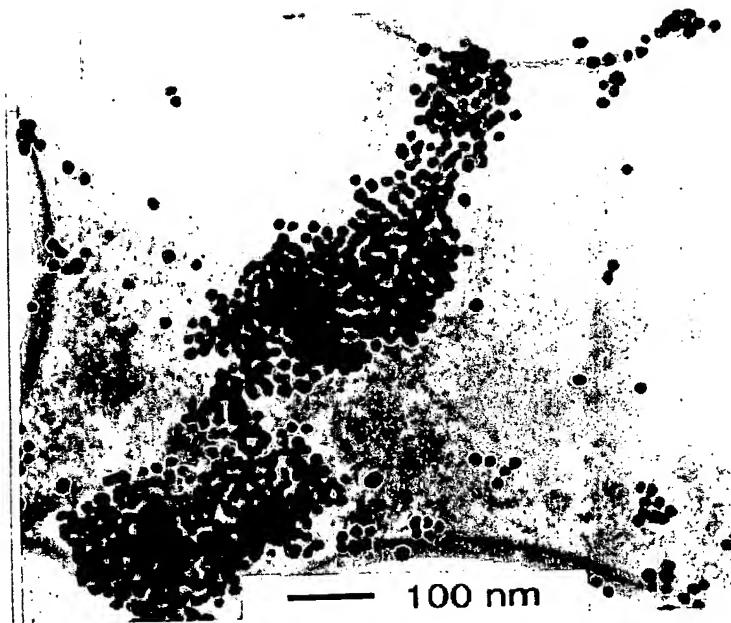
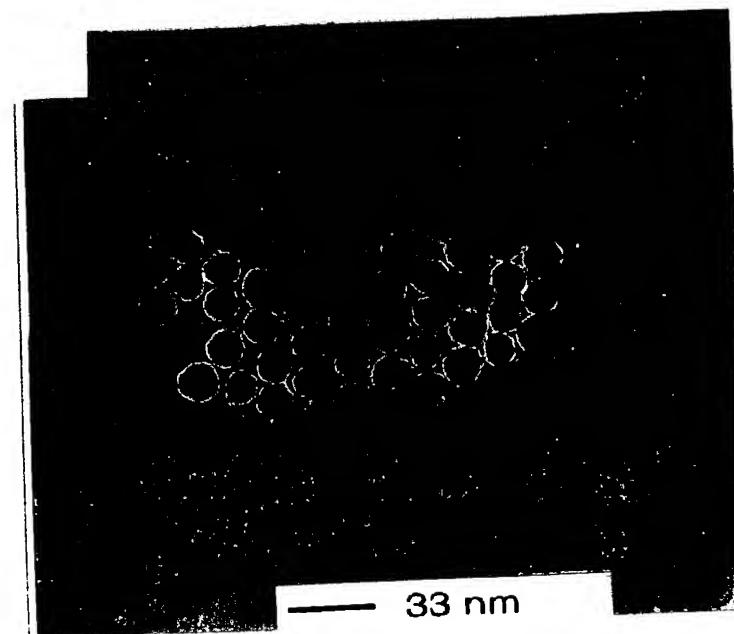


FIG. 9B



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FIG. 10

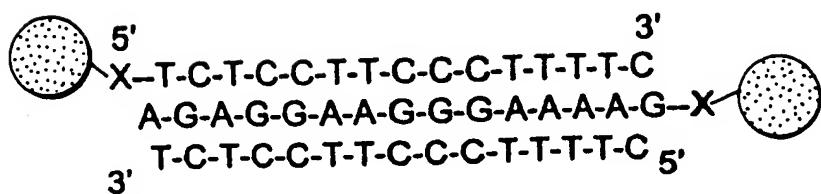
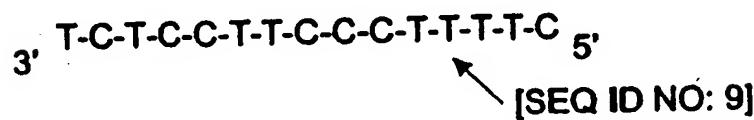
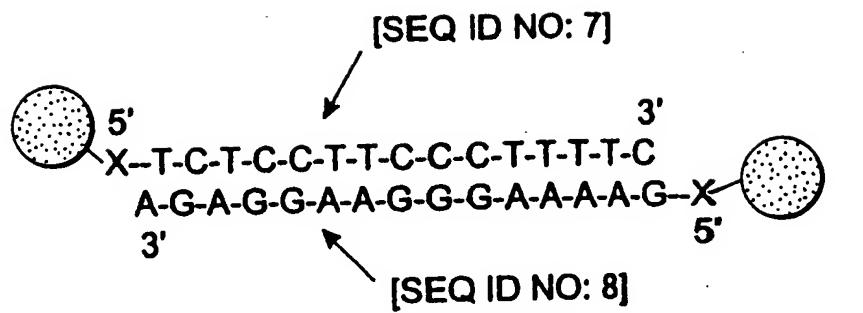


FIG. II

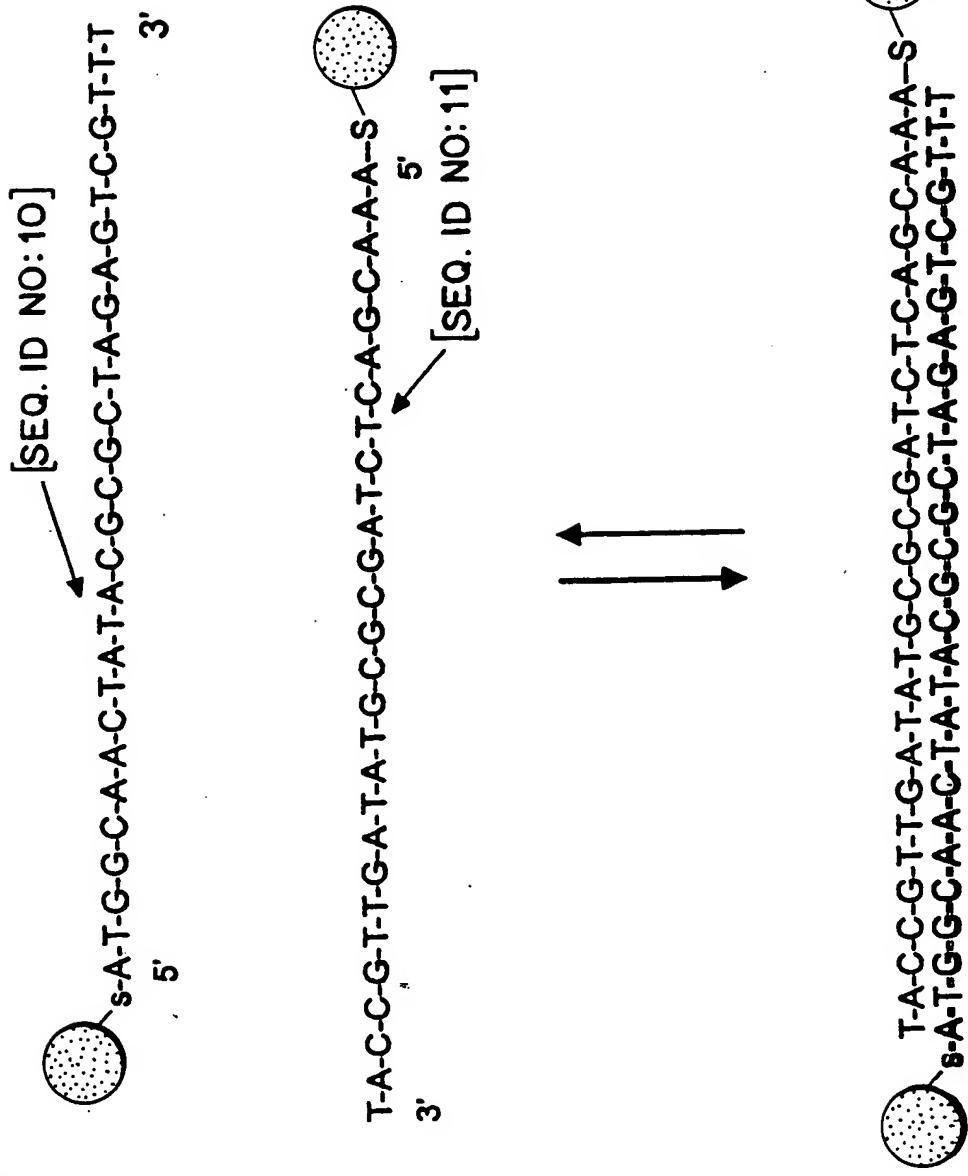


FIG. I2A

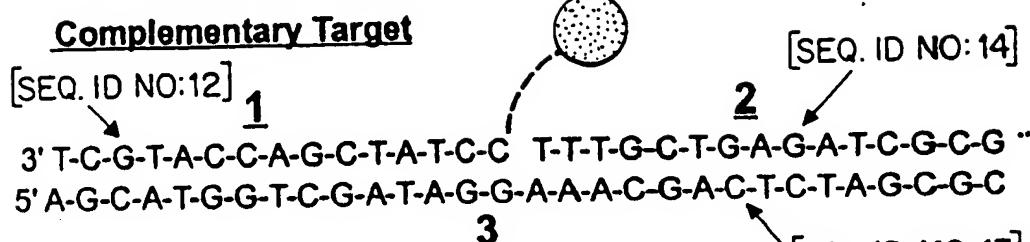


FIG. I2B

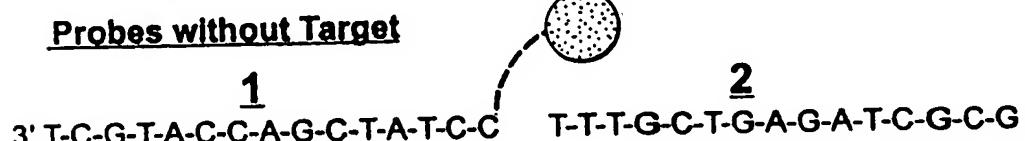


FIG. I2C

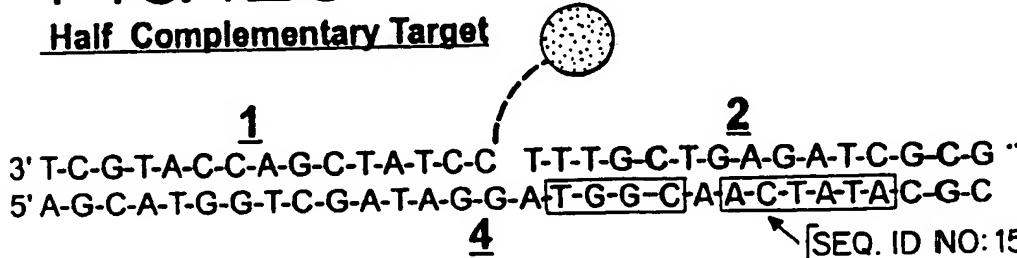


FIG. I2D

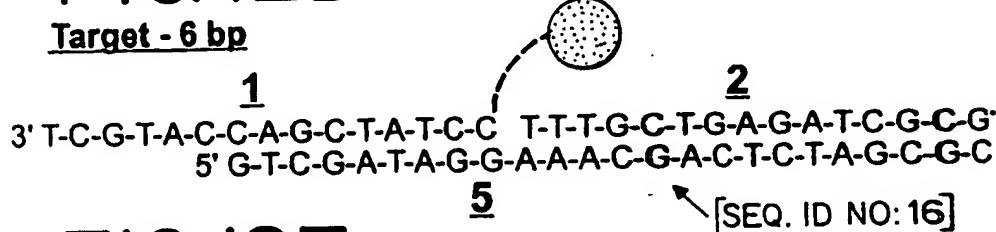


FIG. I2E

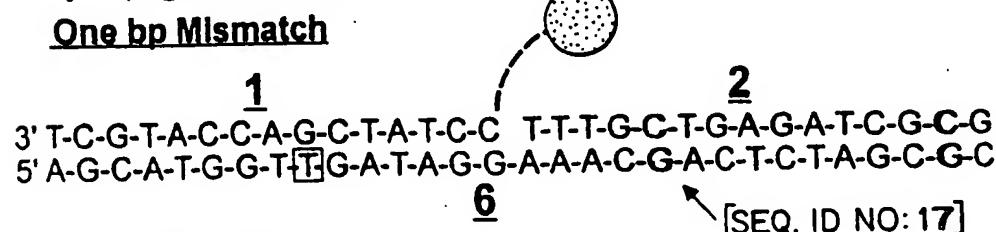


FIG. I2F

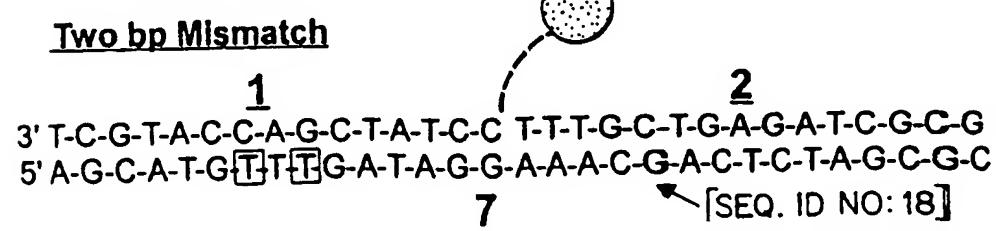
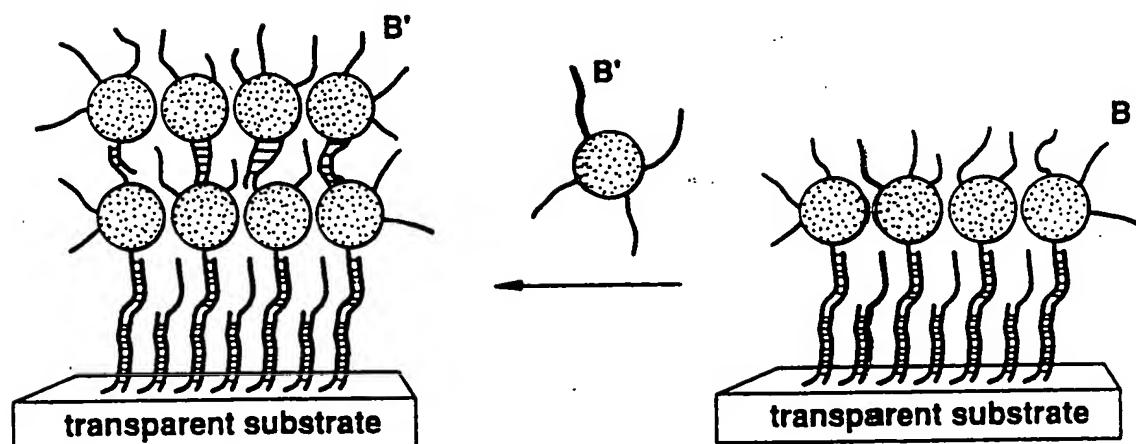
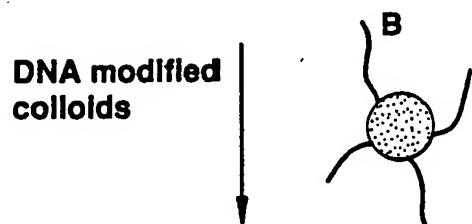
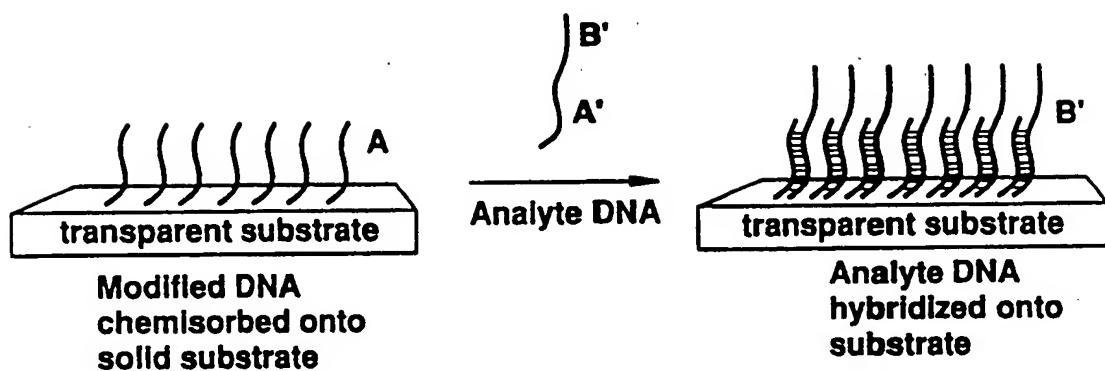


FIG. 13A



Dark areas where nanoparticle aggregates are linked to substrate surface by analyte DNA

DNA modified colloids hybridized to bound analyte DNA

FIG. 13B

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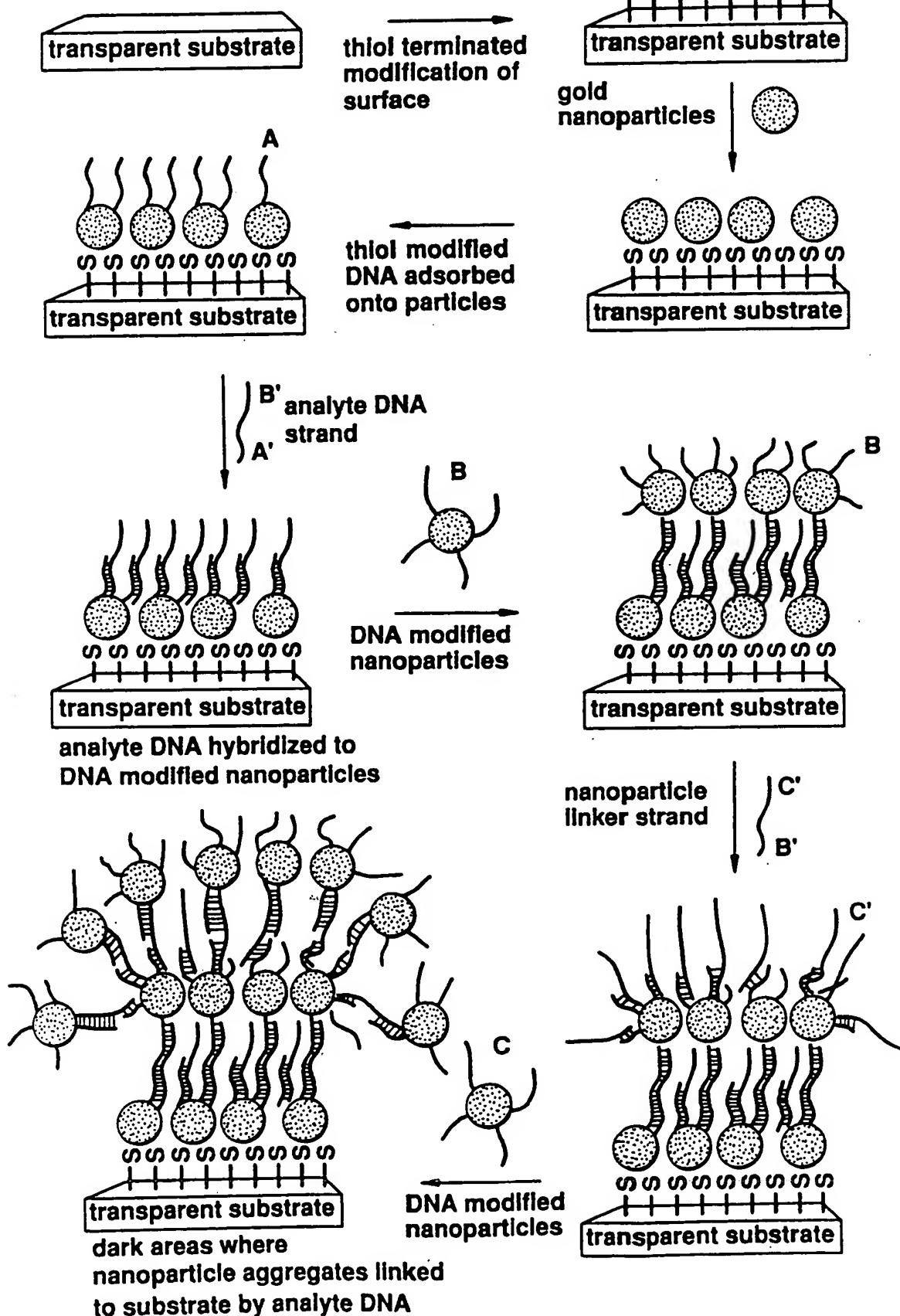


FIG. 14A

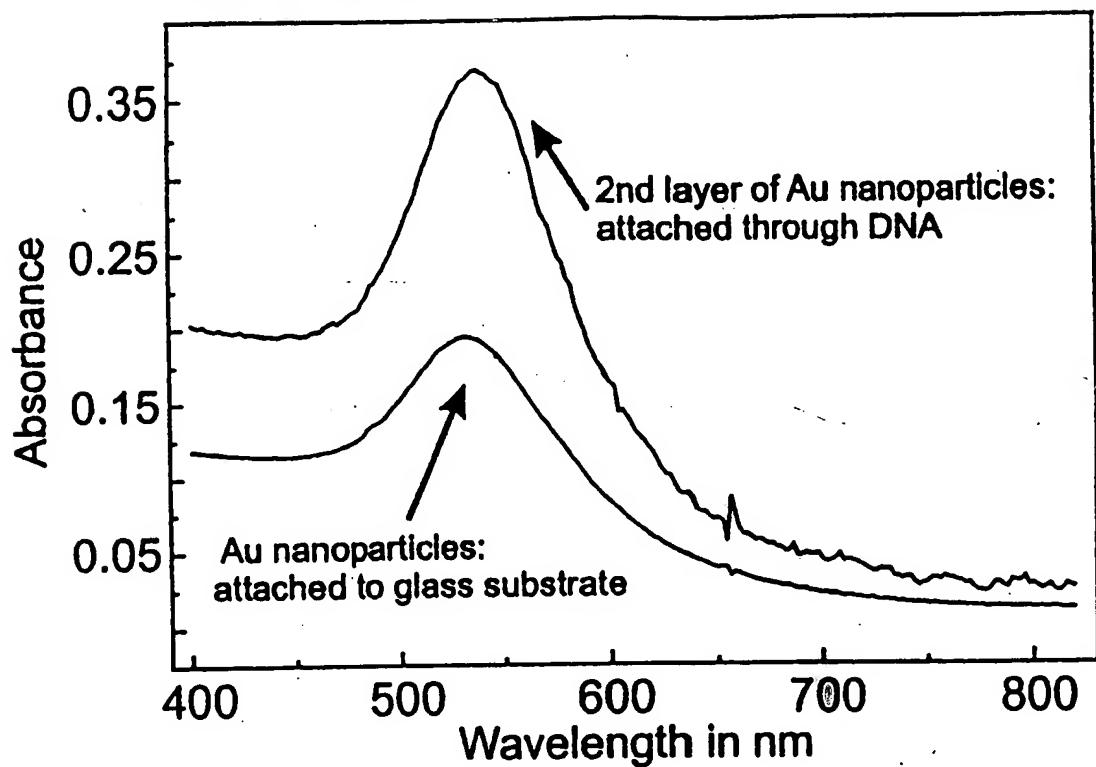


FIG. 14B

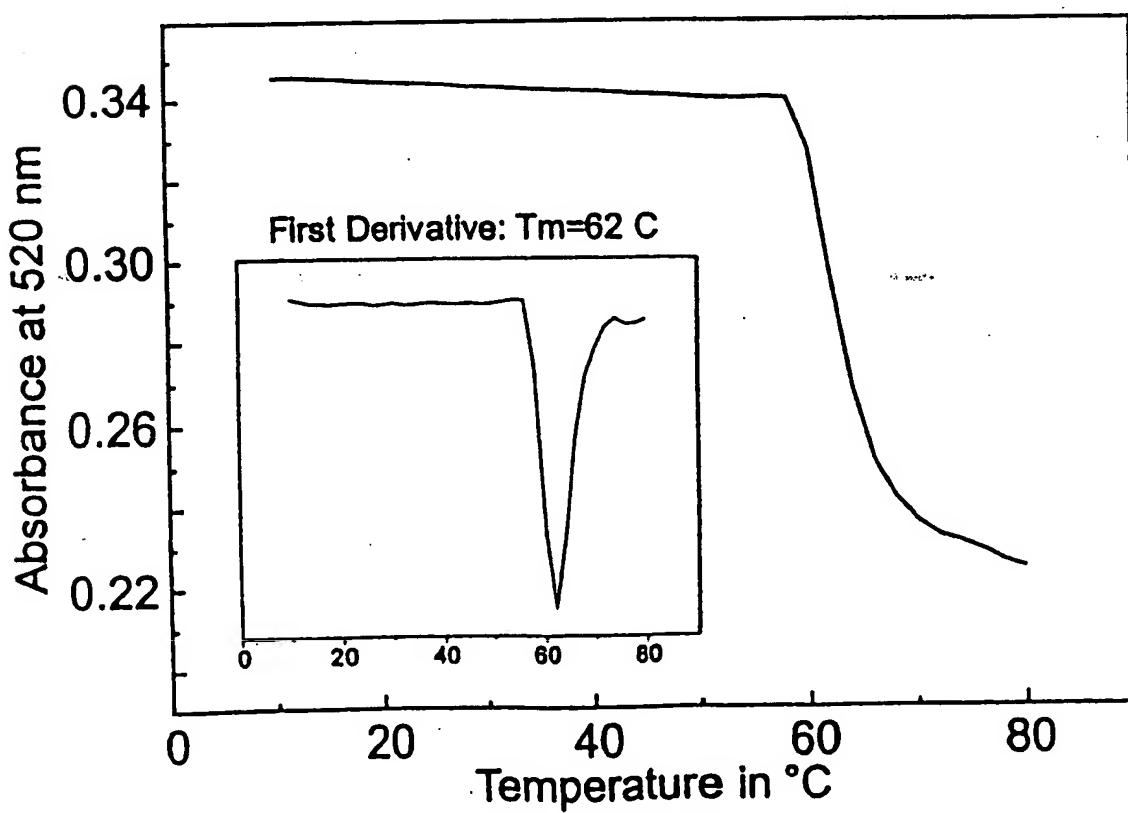
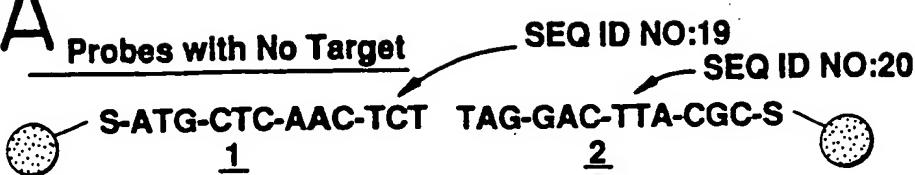
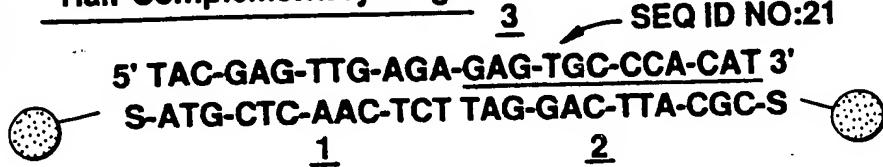
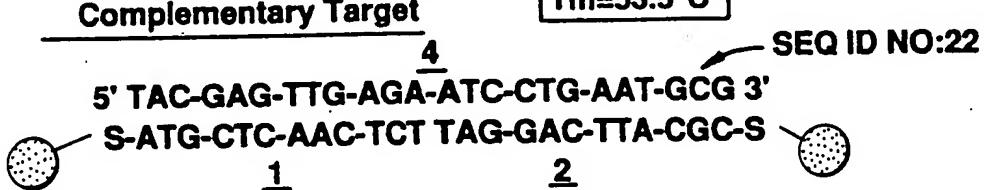
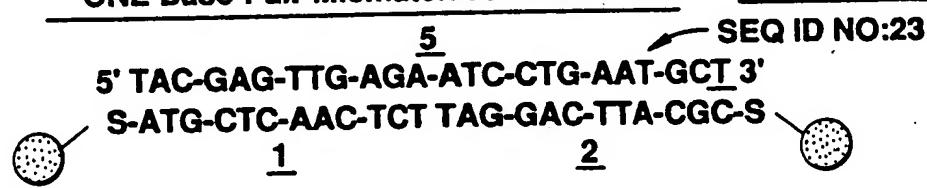
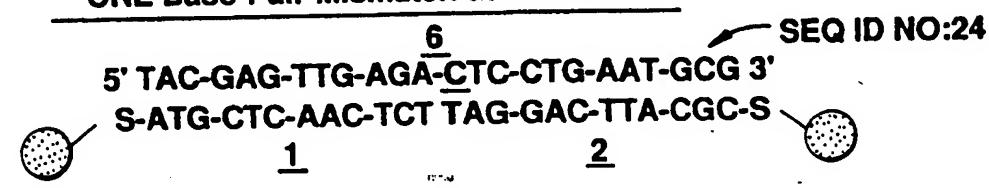


FIG. 15AProbes with No Target**FIG. 15B**Half-Complementary Target**FIG. 15C**Complementary Target $T_m=53.5^\circ C$ **FIG. 15D**ONE Base-Pair Mismatch at Probe Head $T_m=50.4^\circ C$ **FIG. 15E**ONE Base-Pair Mismatch at Probe Tail $T_m=46.2^\circ C$ **FIG. 15F**ONE Base Deletion

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SEQ ID NO:25

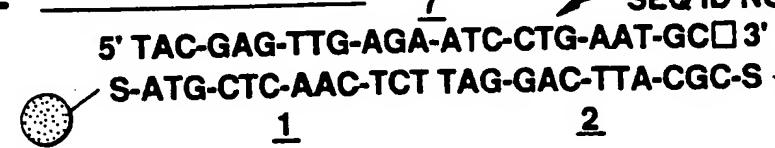
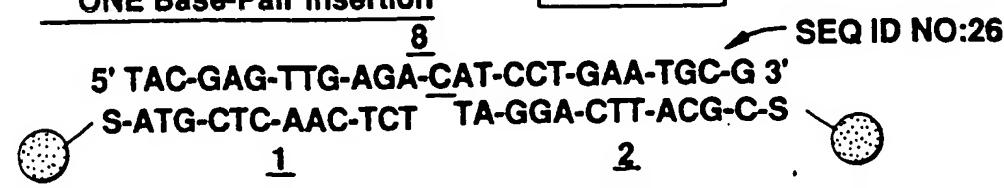
**FIG. 15G**ONE Base-Pair Insertion $T_m=50.2^\circ C$ 

FIG. 16A

24 Base Template

5' TAC-GAG-TTG-AGA-ATC-CTG-AAT-GCG 3'
—S-ATG-CTC-AAC-TCT TAG-GAC-TTA-CGC-S —
1
2

FIG. 16B

48 Base Template with Complementary 24 Base Filler

5' TAC-GAG-TTG-AGA-CCG-TTA-AGA-CGA-GCG-AAT-CAT-GCA-ATC-CTG-AAT-GCG 3'
—S-ATG-CTC-AAC-TCT GGC-AAT-TCT-GCT-CCG-TTA-GTA-CGT TAG-GAC-TTA-CGC-S —
1
2

FIG. 16C

72 Base Template with Complementary 48 Base Filler

5' TAC-GAG-TTG-AGA-CCG-TTA-AGA-CGA-GCG-AAT-CAT-GCA-TAT-ATT-GGA-CGC-TTT-ACG-GAC-AAC-ATC-CTG-AAT-GCG 3'
—S-ATG-CTC-AAC-TCT GGC-AAT-TCT-GCT-CCG-TTA-GTA-CGT-ATA-TAA-CCT-GCG-AAA-TGC-CTG-TTG TAG-GAC-TTA-CGC-S —
1
2

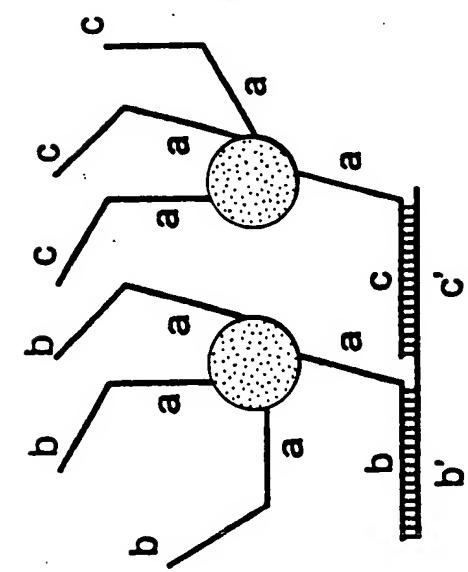
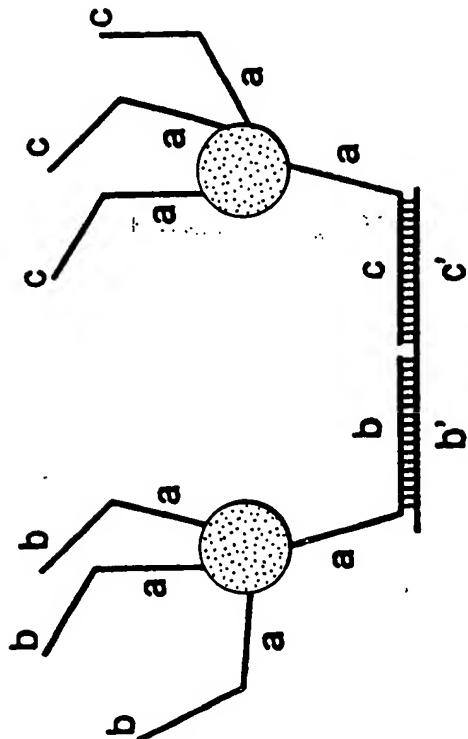
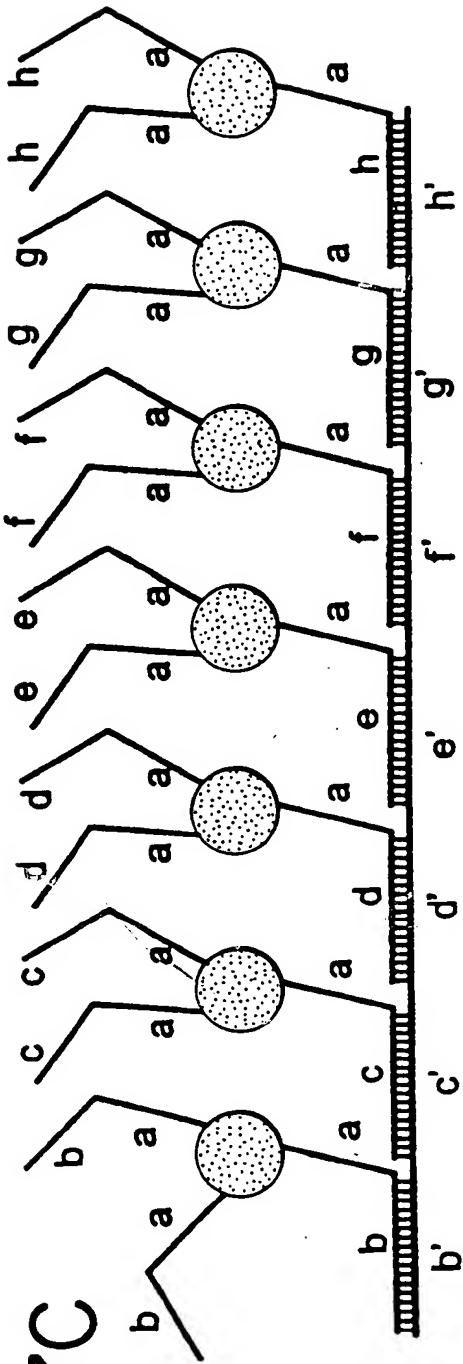
FIG. 17B**FIG. 17C**

FIG. 17D

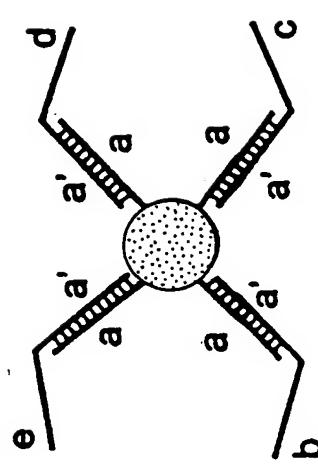
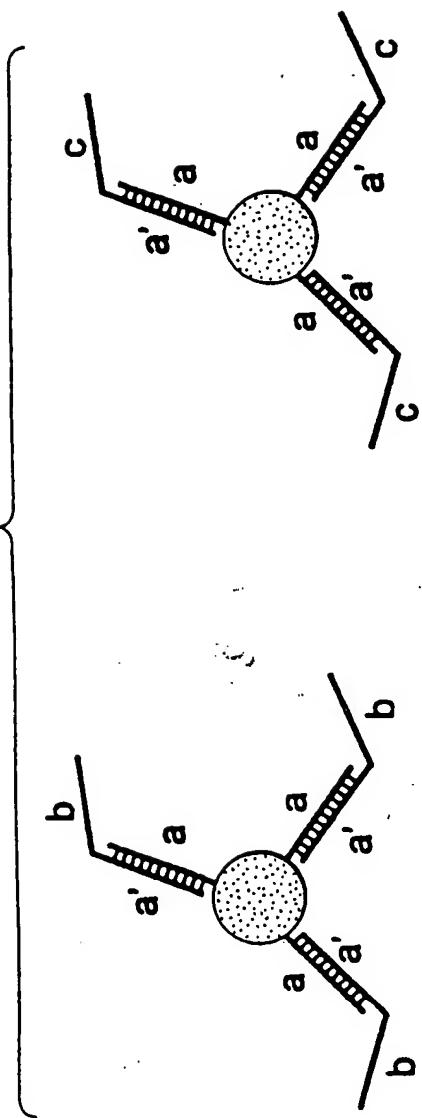
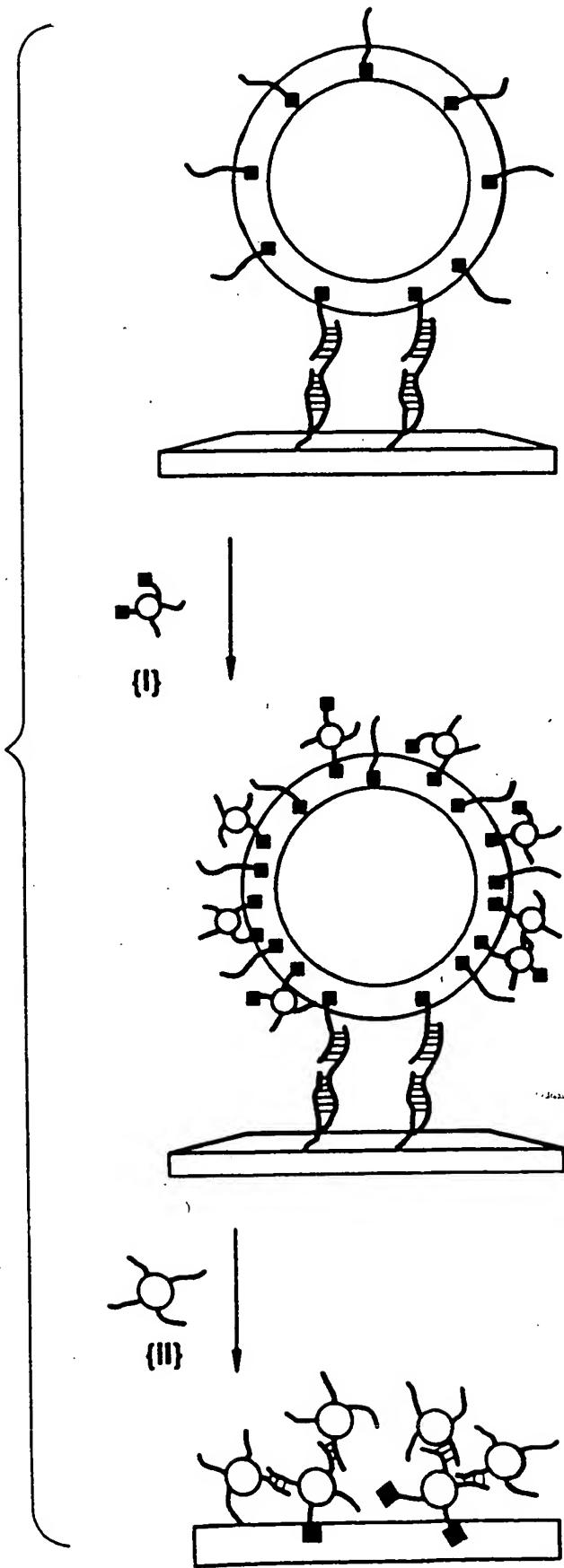


FIG. 17E

FIG. 18

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FIG. 19A

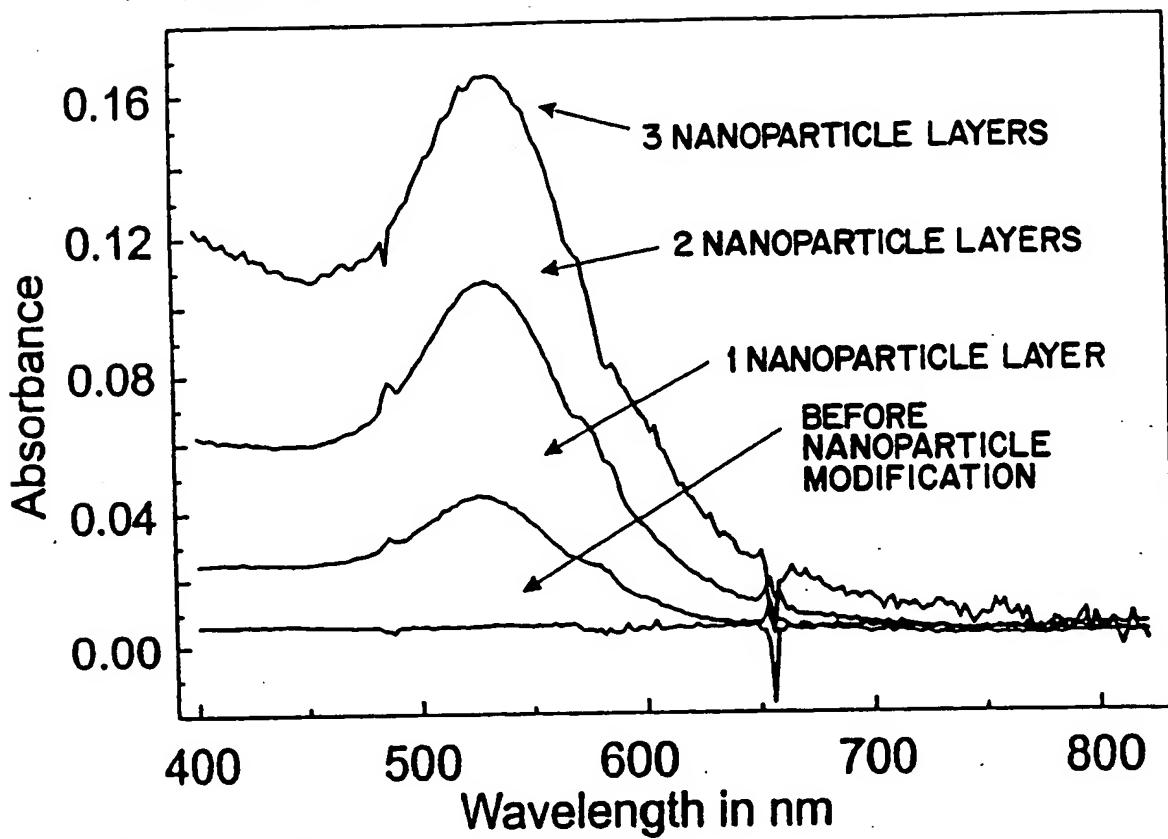
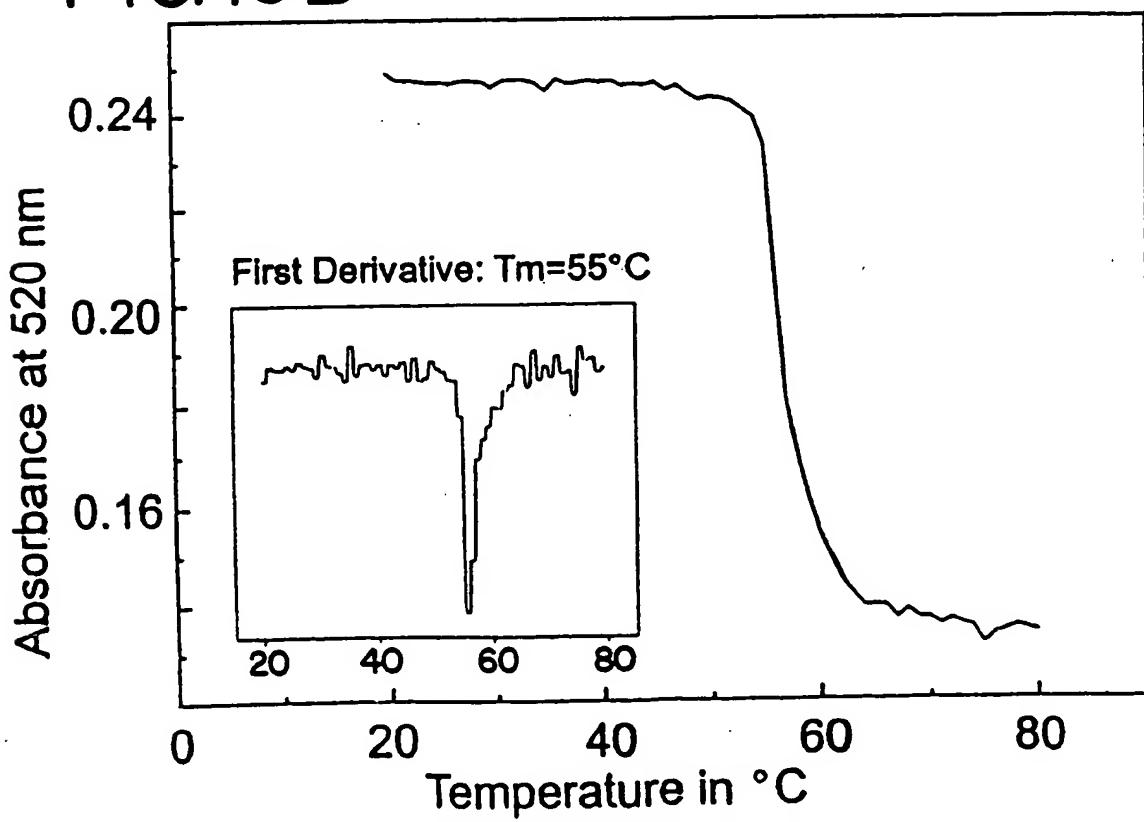


FIG. 19B



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FIG. 20A

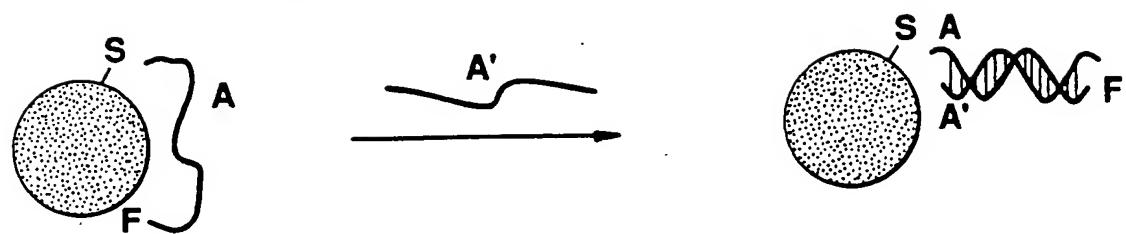


FIG. 20B

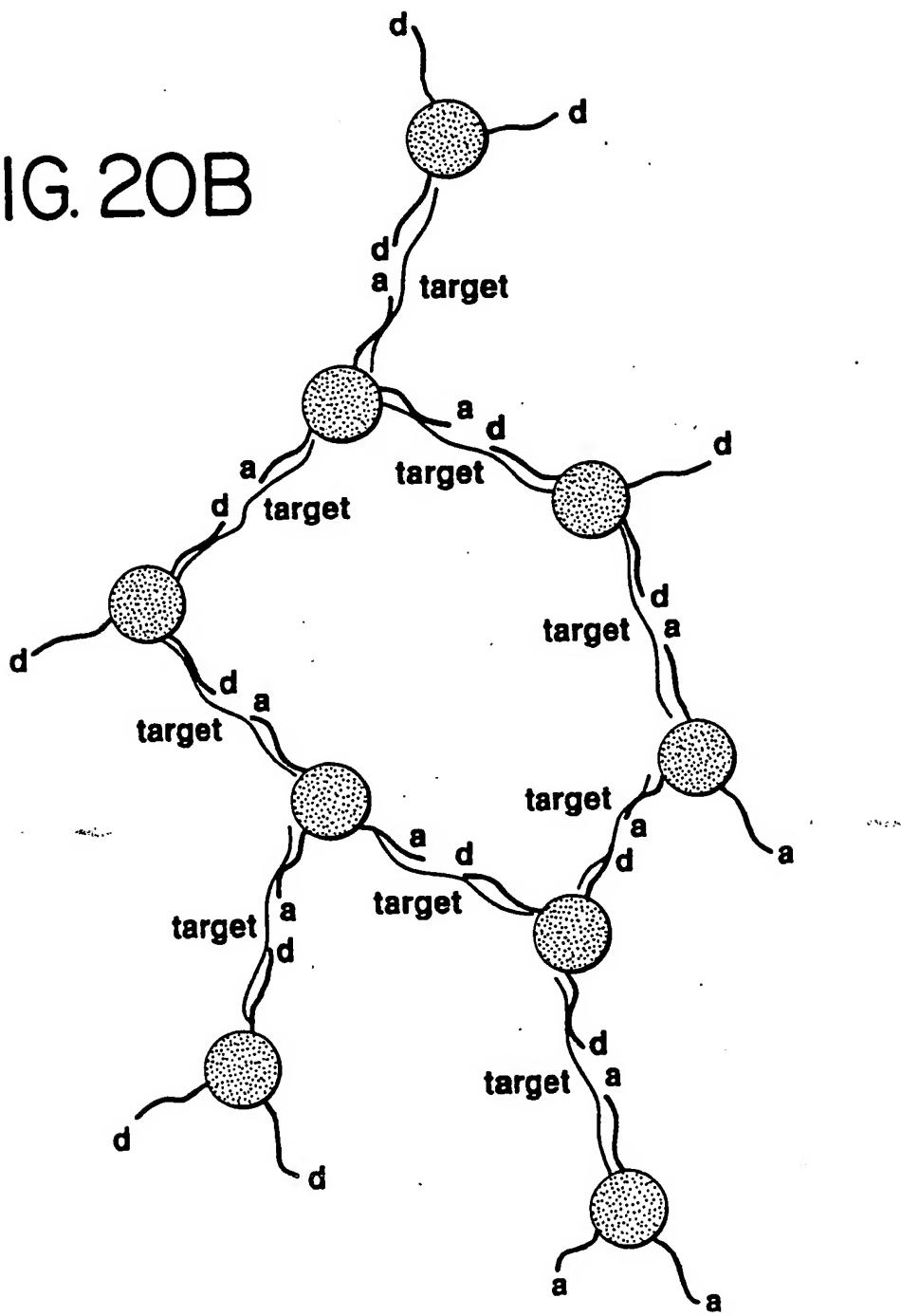


FIG. 2

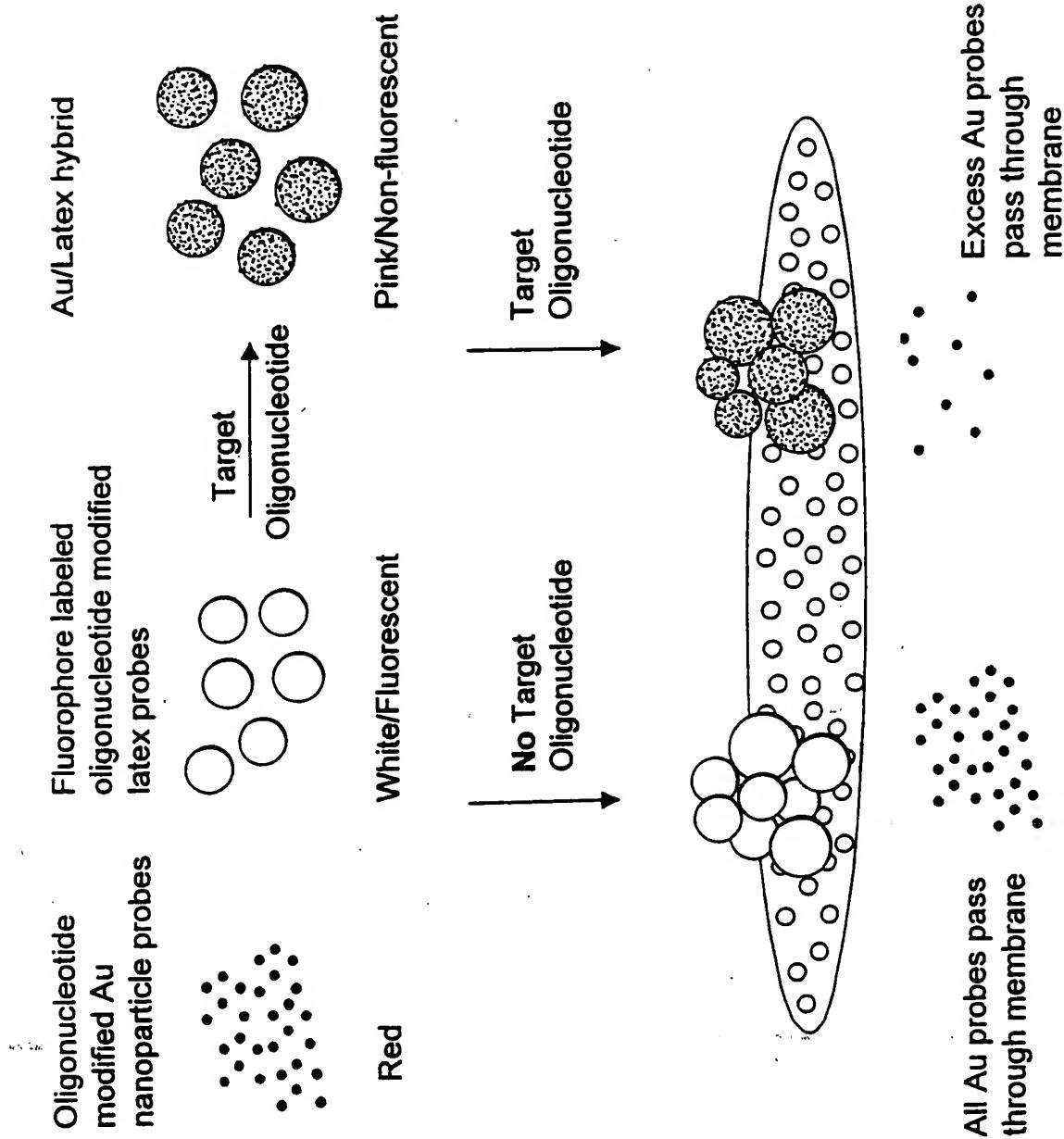
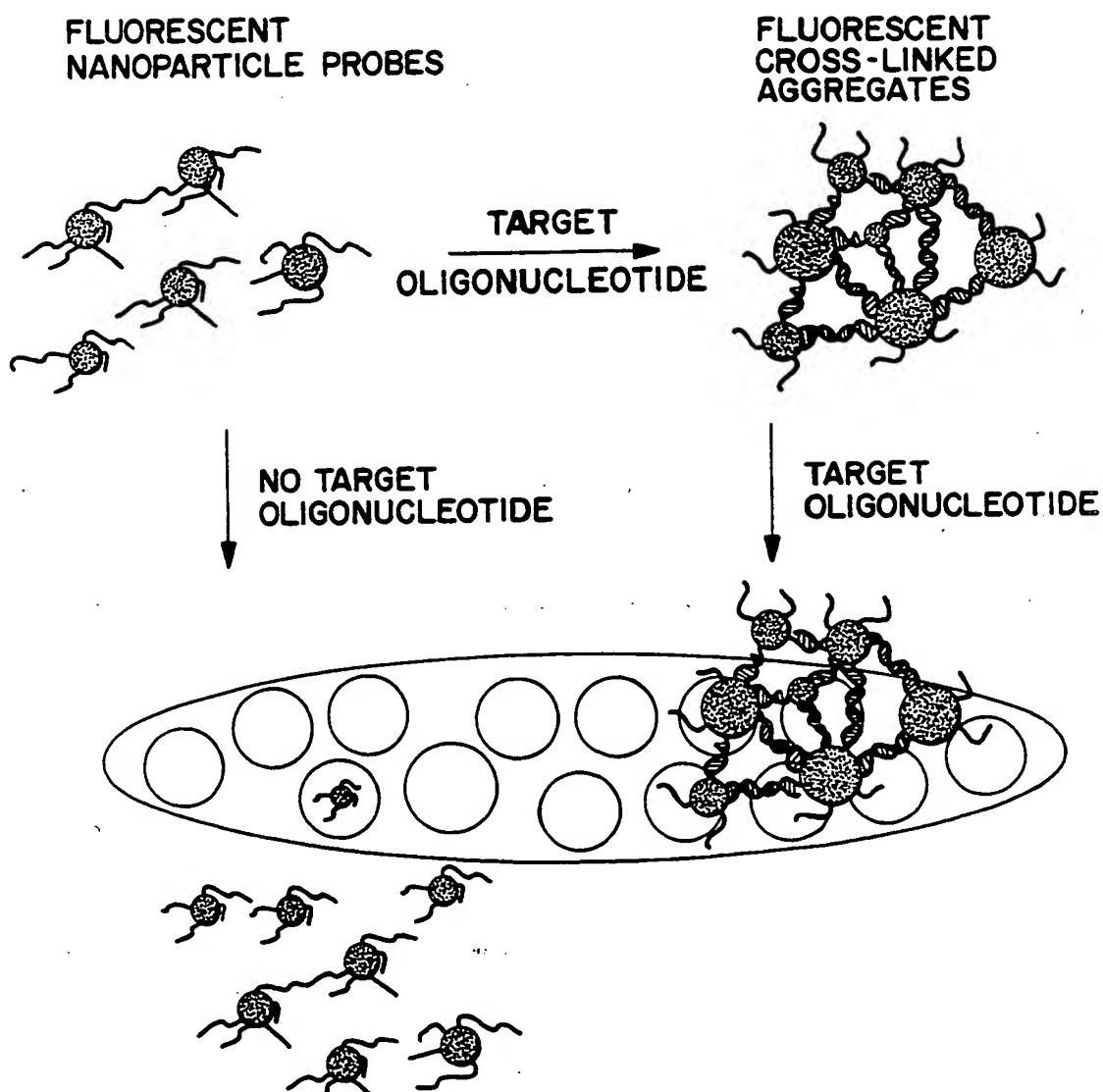


FIG. 22



THE FLUORESCENT NANOPARTICLE
PROBES PASS THROUGH THE
MEMBRANE

THE FLUORESCENT
CROSS-LINKED AGGREGATES
ARE RETAINED BY THE
MEMBRANE

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FIG. 23

Anthrax PCR Product

5' G GCG GAT GAG TCA GTA GTT AAG GAG GCT CAT AGA GAA GTA ATT AAT
3' C CGC CTA CTC AGT CAT CAA TTC CTC CGA GTA TCT CTT CAT TAA TTA

TCG TCA ACA GAG GGA TTA TTG TTA AAT ATT GAT AAG GAT ATA AGA AAA
AGC AGT TGT CTC CCT AAT AAC AAT TTA TAA CTA TTC CTA TAT TCT TTT

ATA TTA TCC AGG GTT ATA TTG TAG AAA TTG AAG ATA CTG AAG GGC TT 3'
TAT AAT AGG TCC CAA TAT AAC ATC TTT AAC TTC TAT GAC TTC CCG AA 5'

141 mer Anthrax PCR product [SEQ ID NO:36]

3' CTC CCT AAT AAC AAT

[SEQ ID NO:37]

3' TTA TAA CTA TTC CTA

[SEQ ID NO:38]

Oligonucleotide-Nanoparticle Probes

Blocker Oligonucleotides

3' C CGC CTA CTC AGT CAT CAA TTC CTC CGA GT
3' A TCT CTT CAT TAA TTA AGC AGT TGT
3' TAT TCT TTT TAT AAT AGG TCC CAA TAT
3' AAC ATC TTT AAC TTC TAT GAC TTC CCG AA

[SEQ ID NO:39]

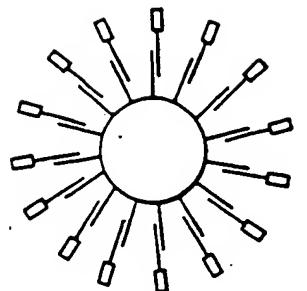
[SEQ ID NO:40]

[SEQ ID NO:41]

[SEQ ID NO:42]

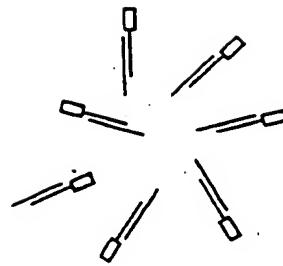
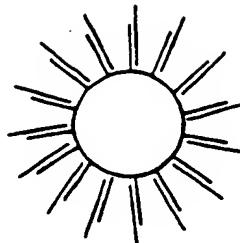
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FIG. 24

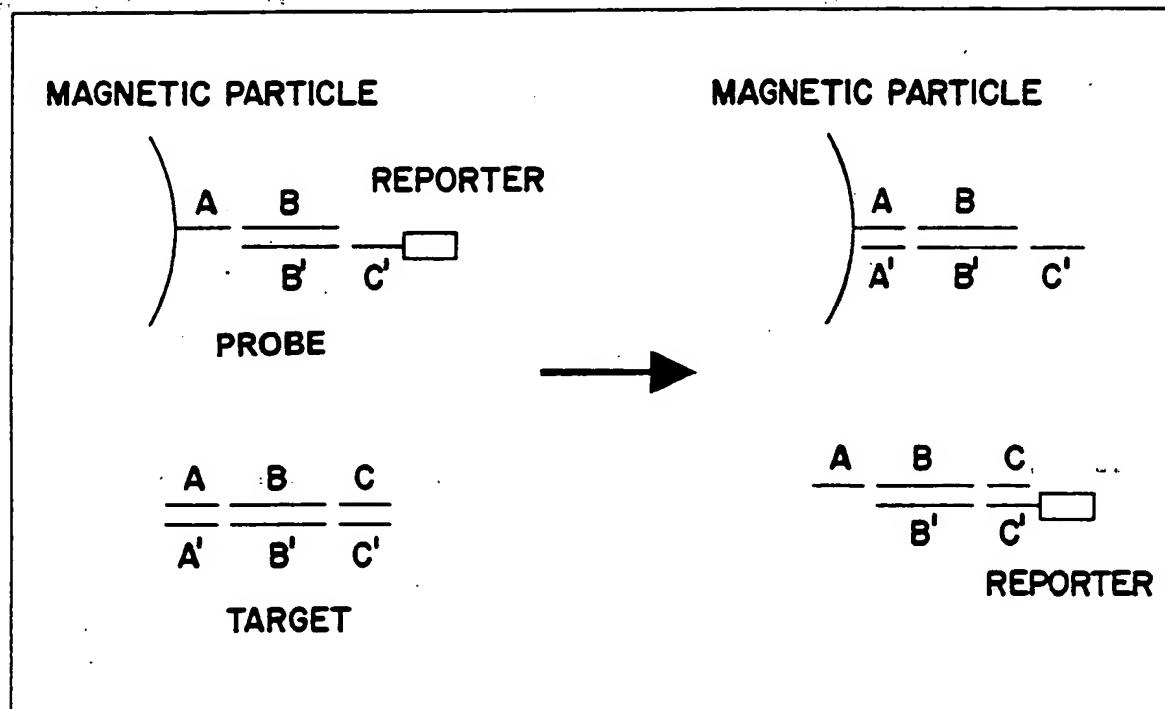


SATELLITE PROBE

TARGET
→



DETECTION SIGNAL



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FIG. 25A

1. (TARGET)

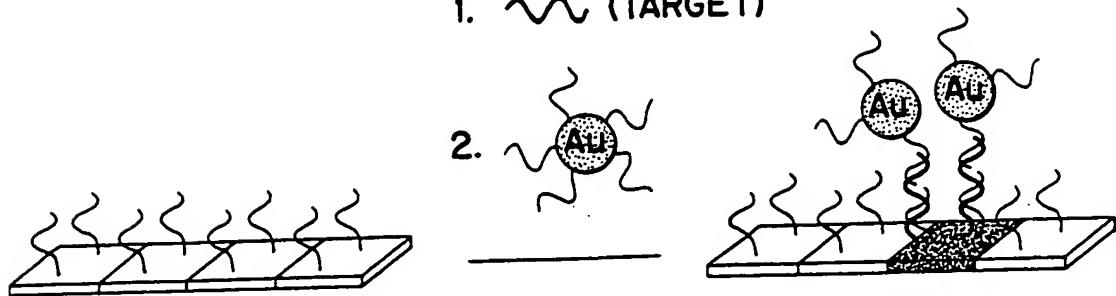
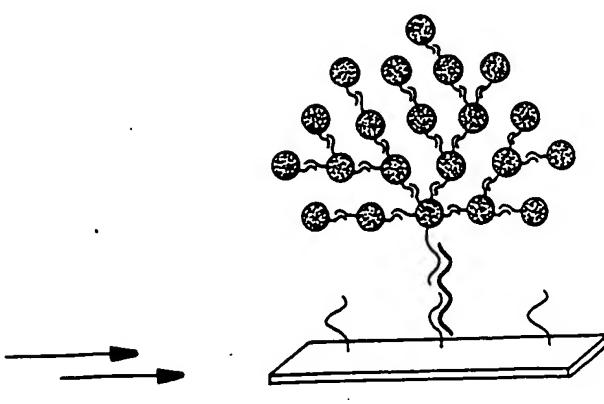
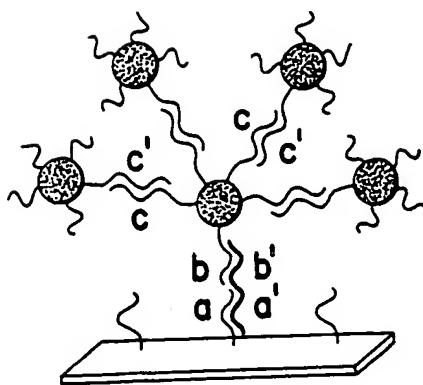
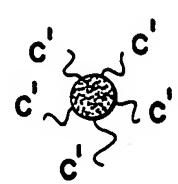
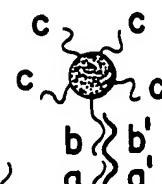
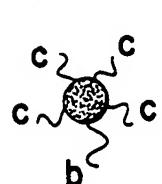
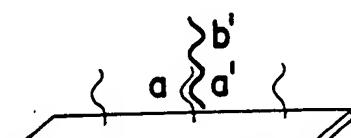
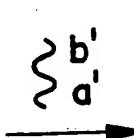
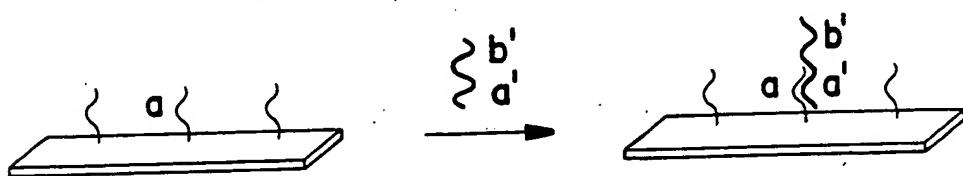


FIG. 25B



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FIG. 26A

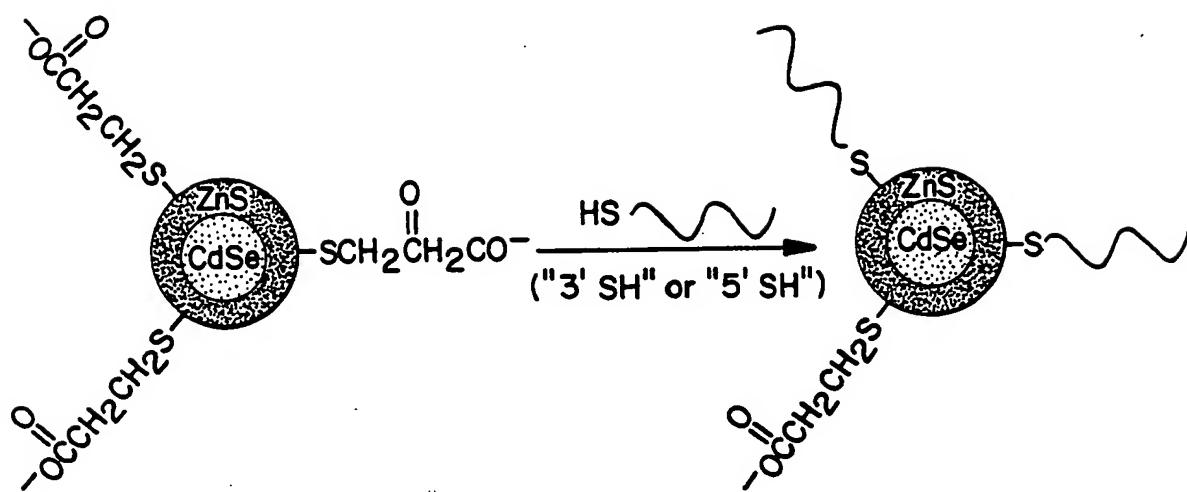


FIG. 26B

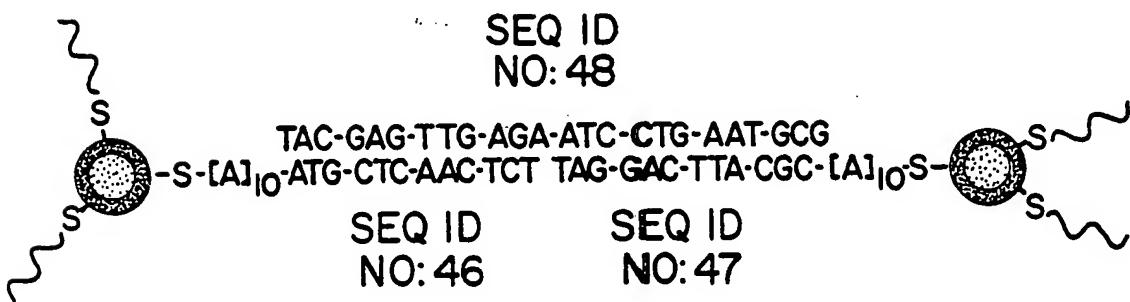


FIG. 27A

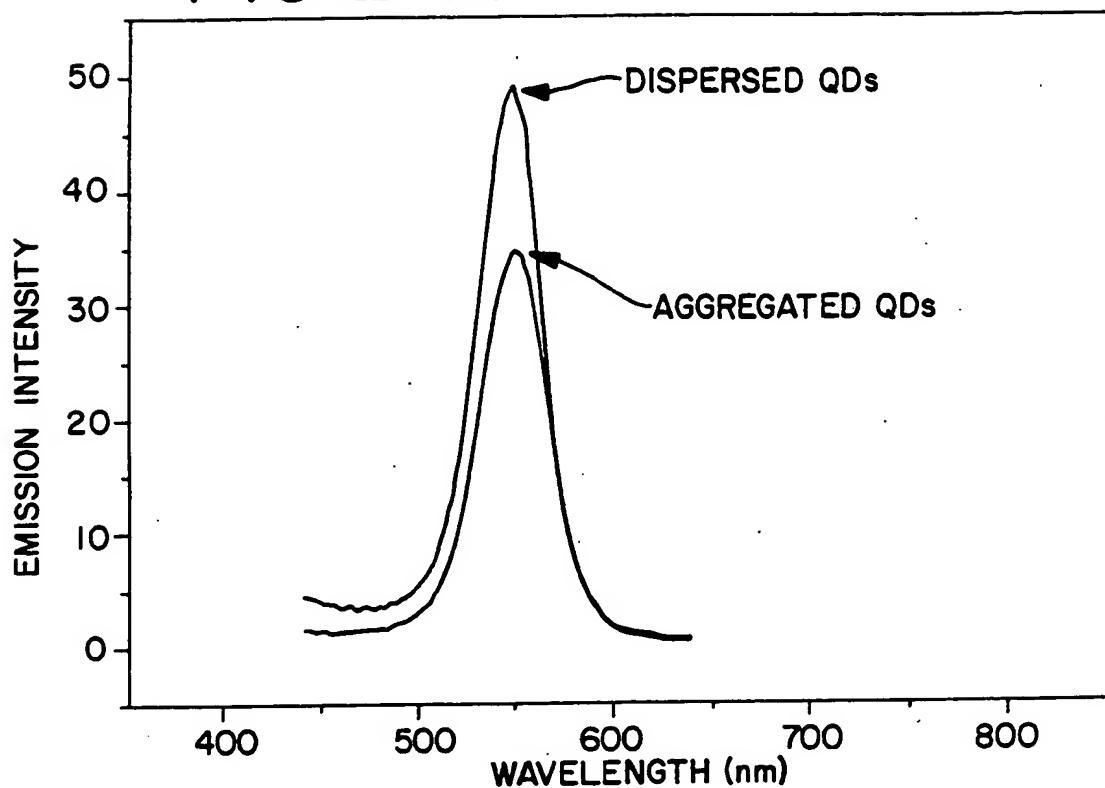
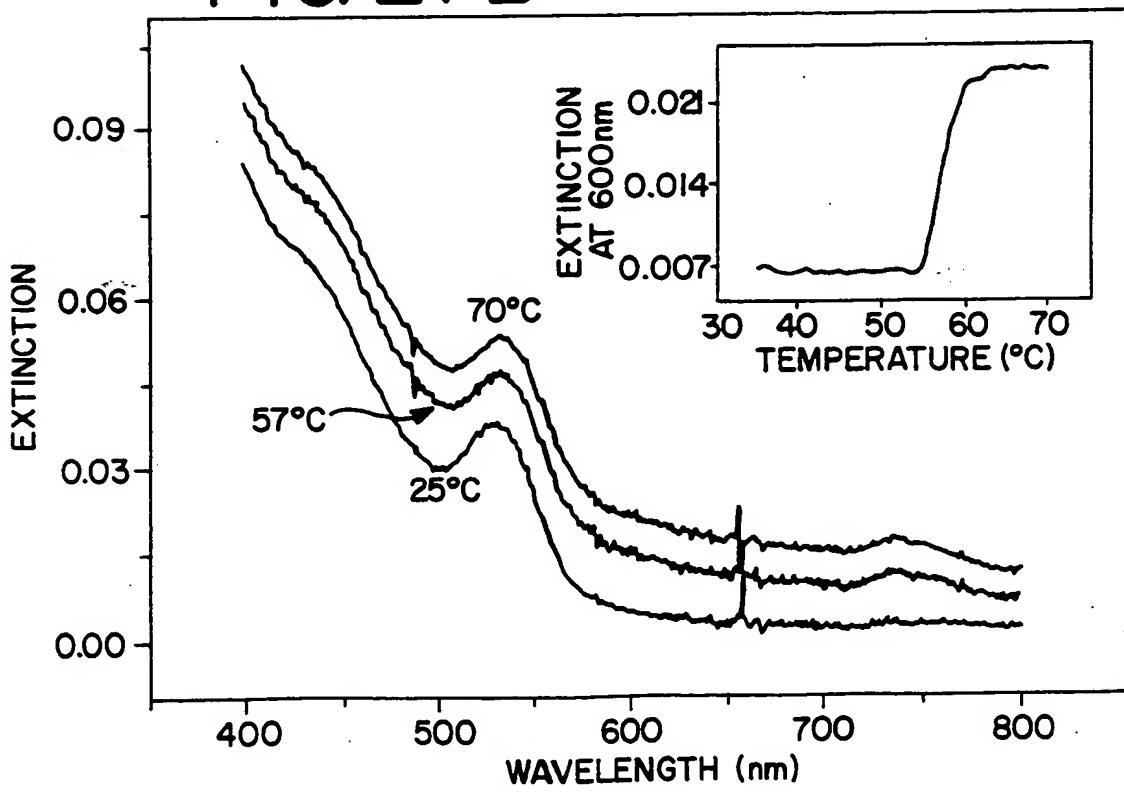


FIG. 27B



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FIG. 27C

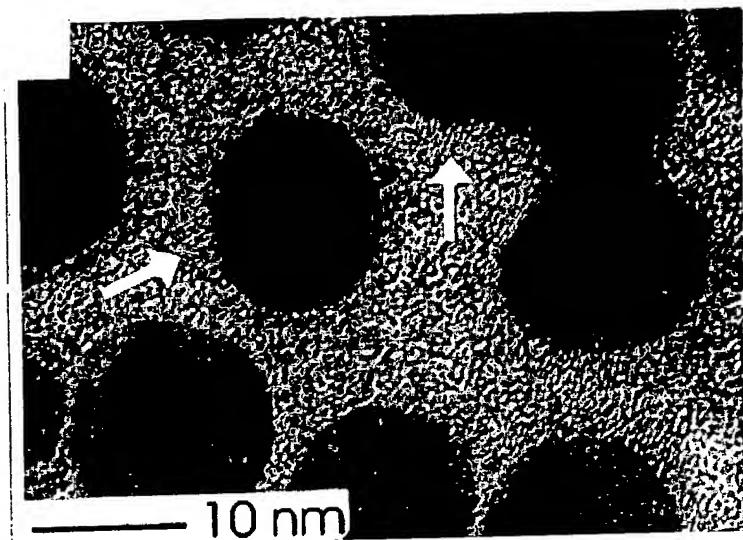


FIG. 27D

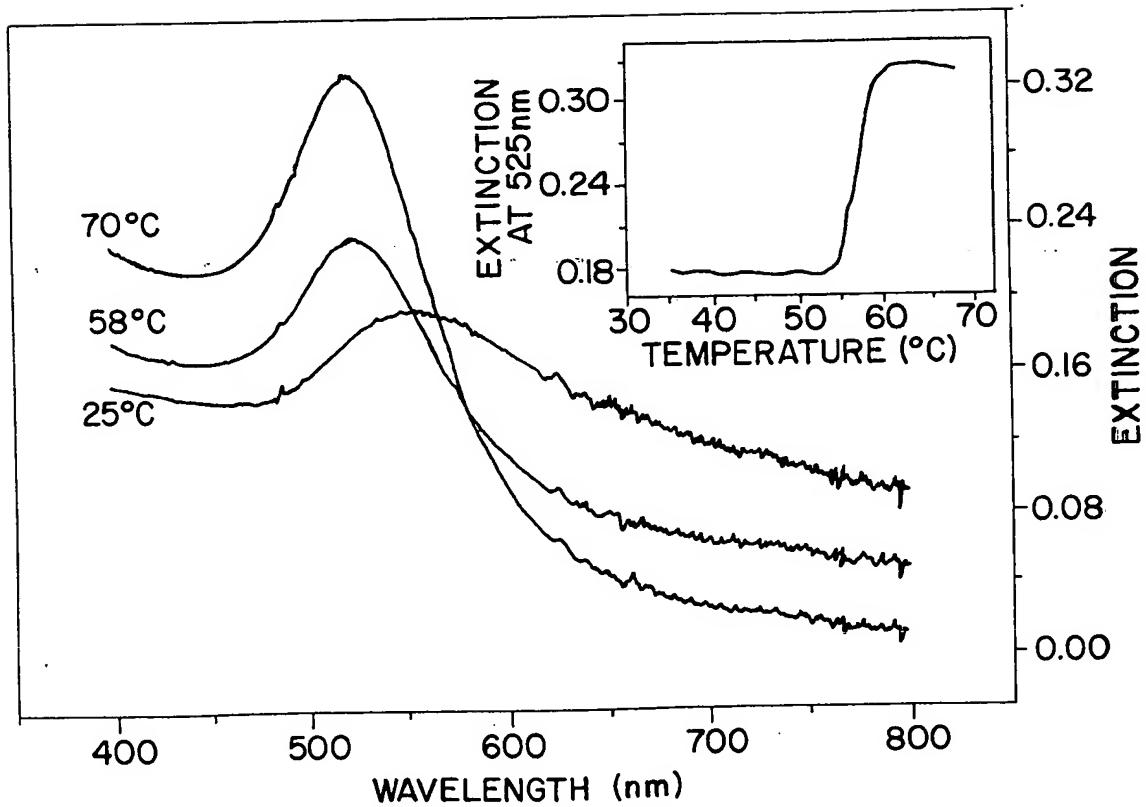


FIG. 28A

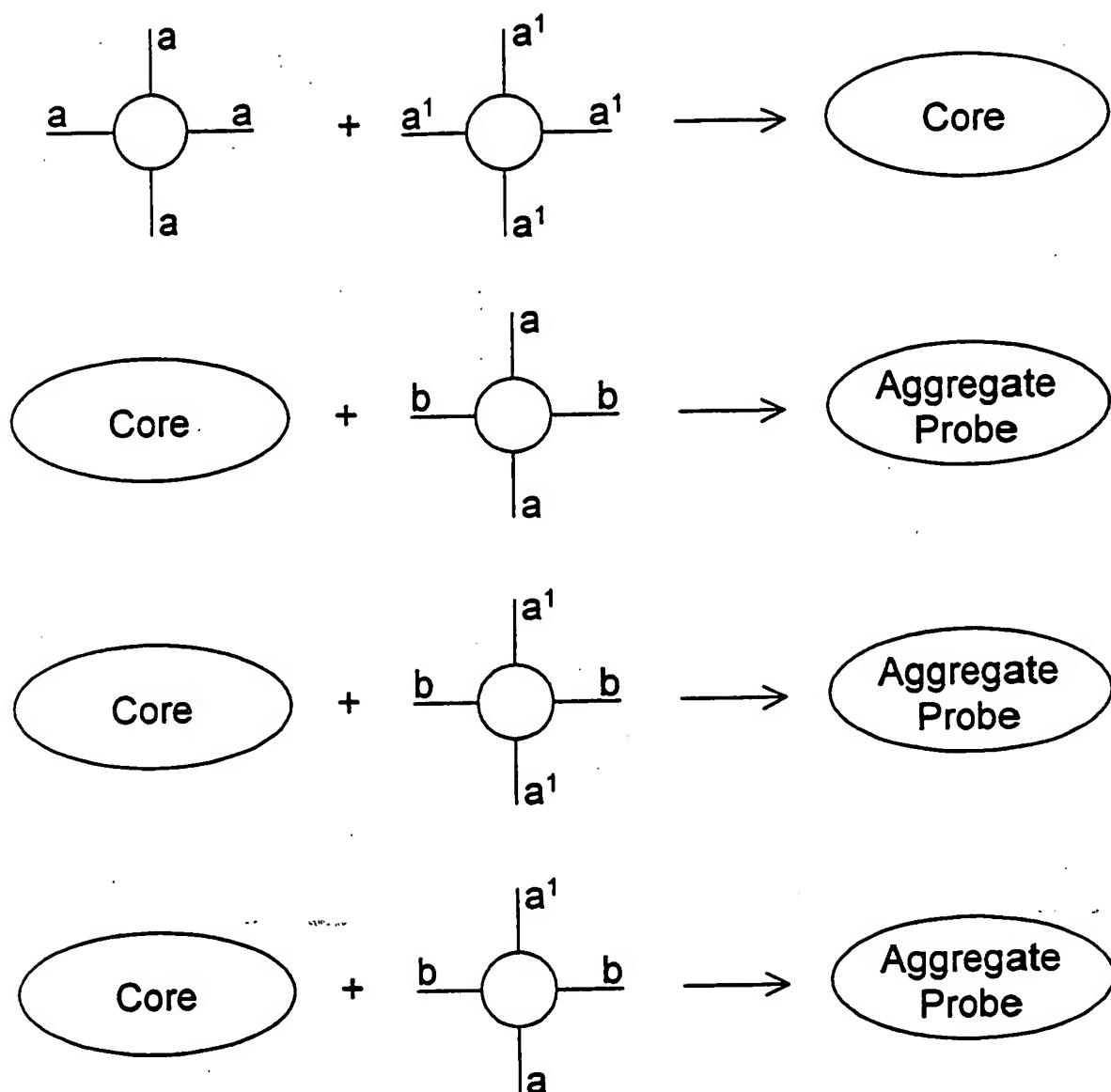


FIG. 28B

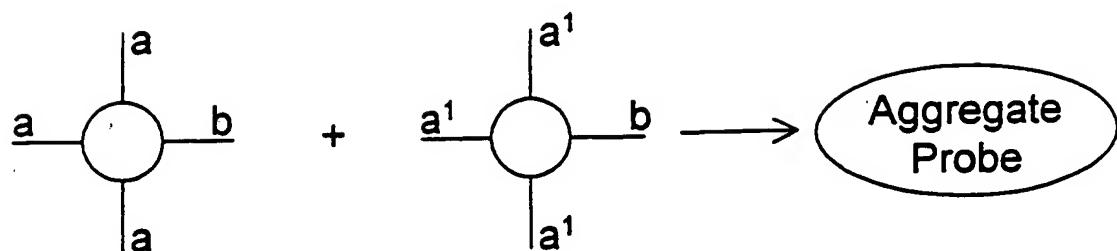


FIG. 28C

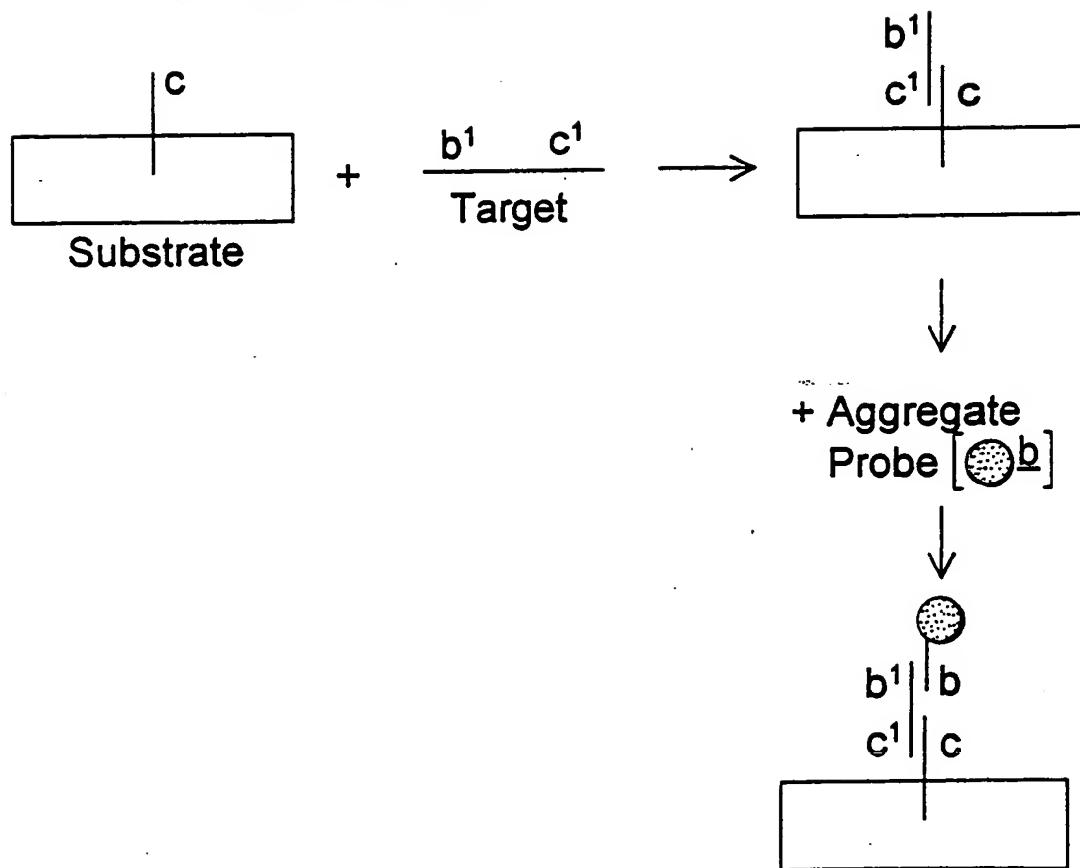


FIG. 28D

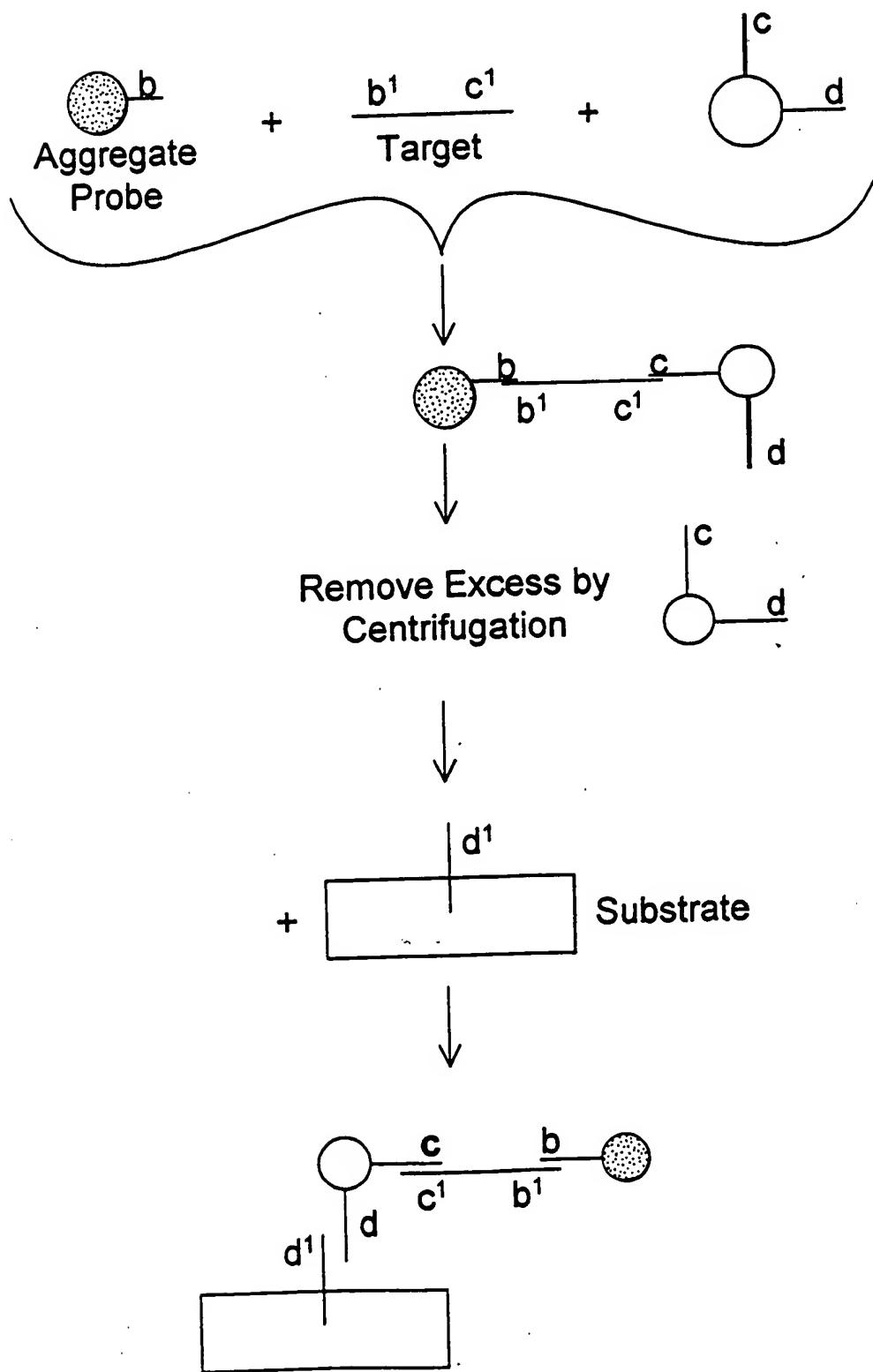


FIG. 28E

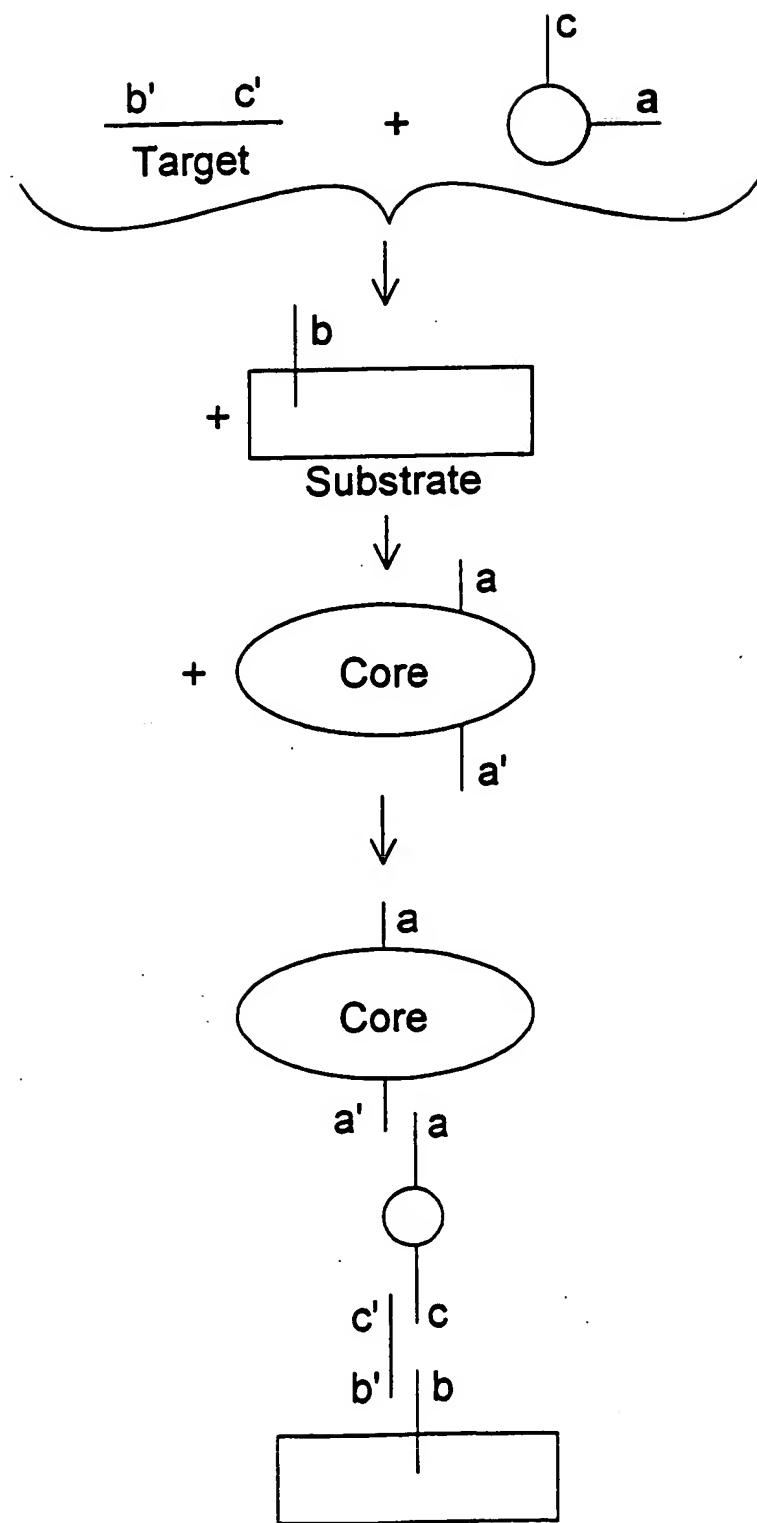


FIG. 29

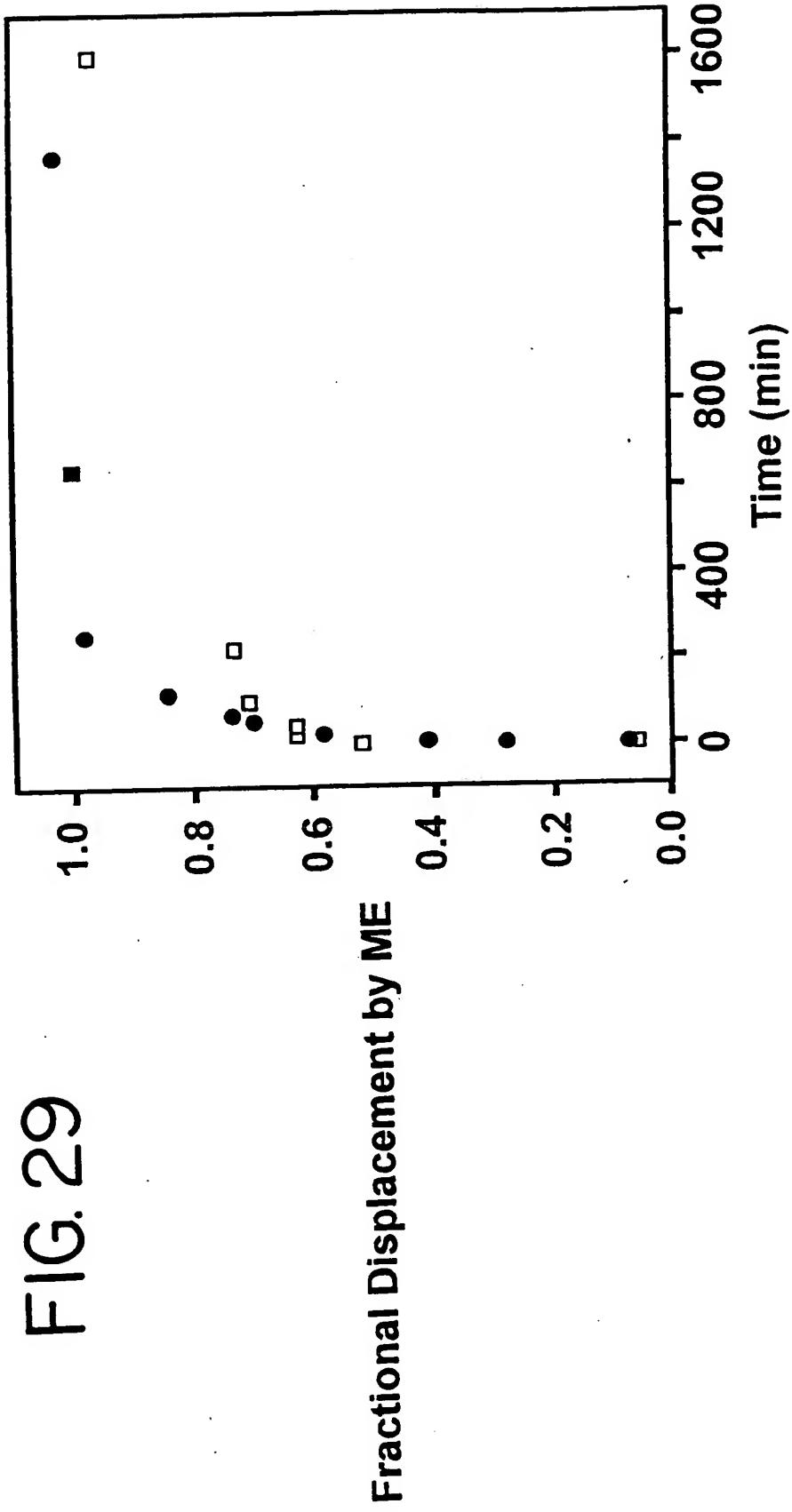


FIG. 30

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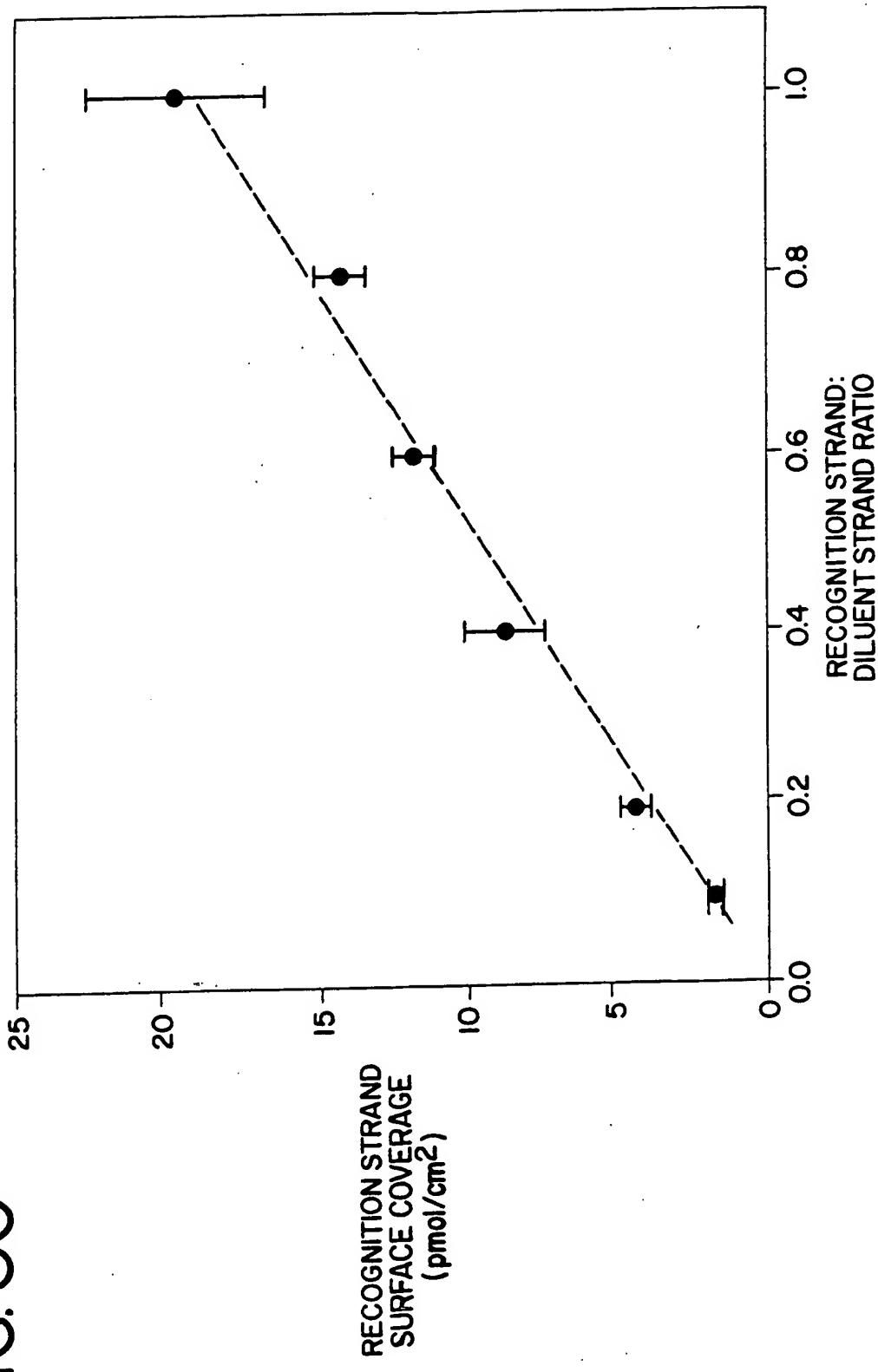


FIG. 3

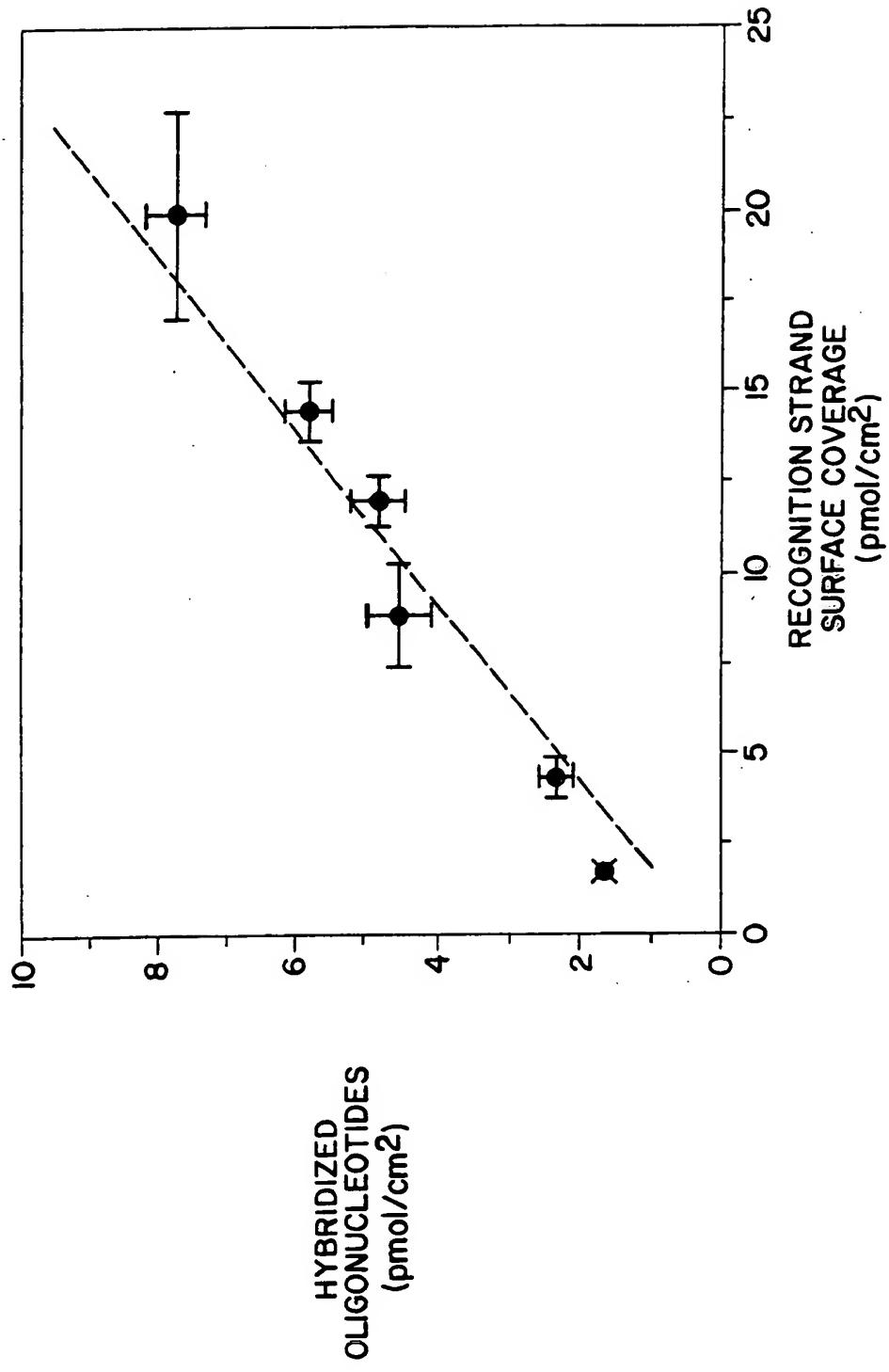
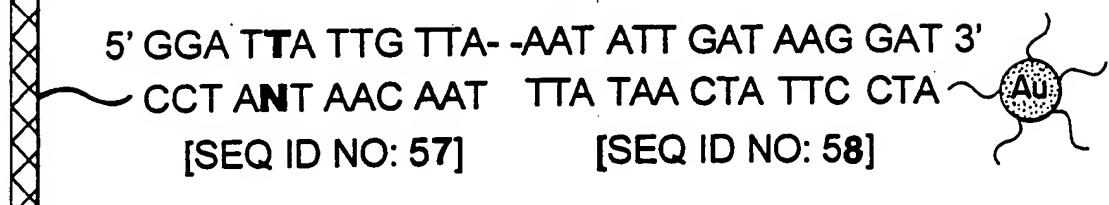
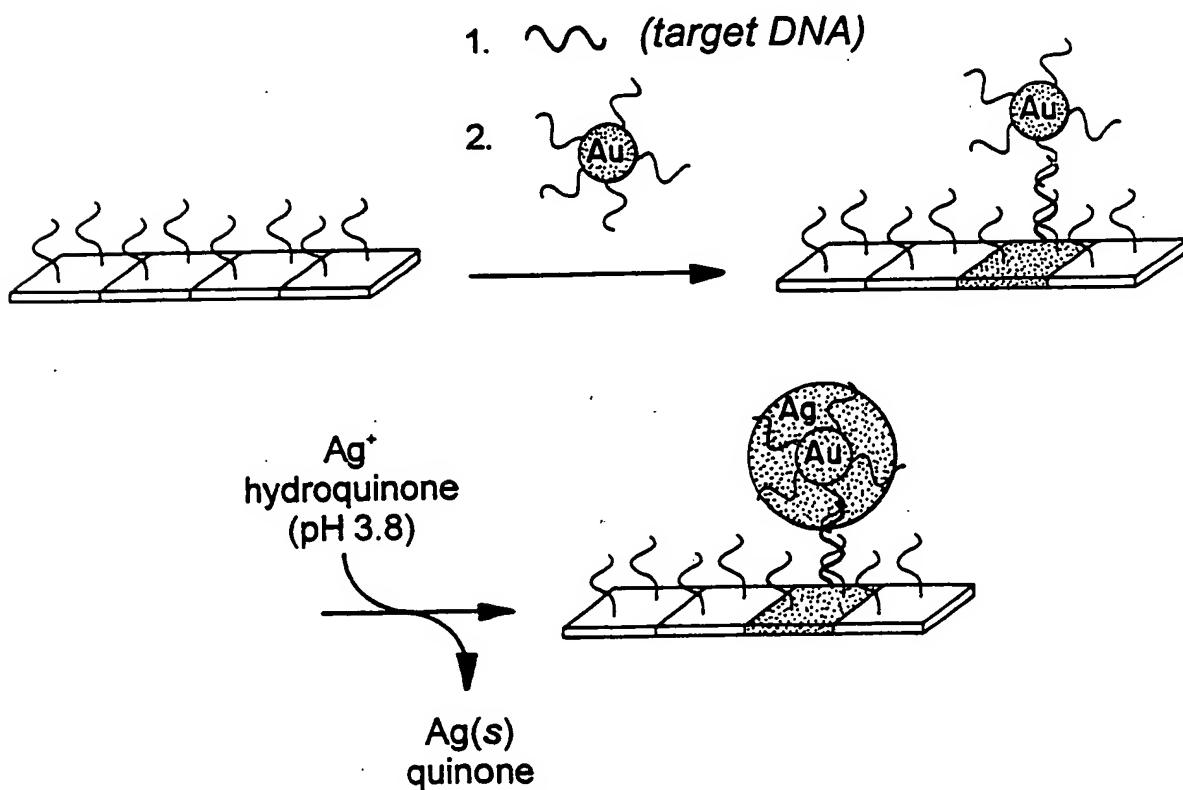


FIG. 32

[SEQ ID NO: 56]



N = A (complementary),
 G,C,T (mismatched)



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FIG. 33

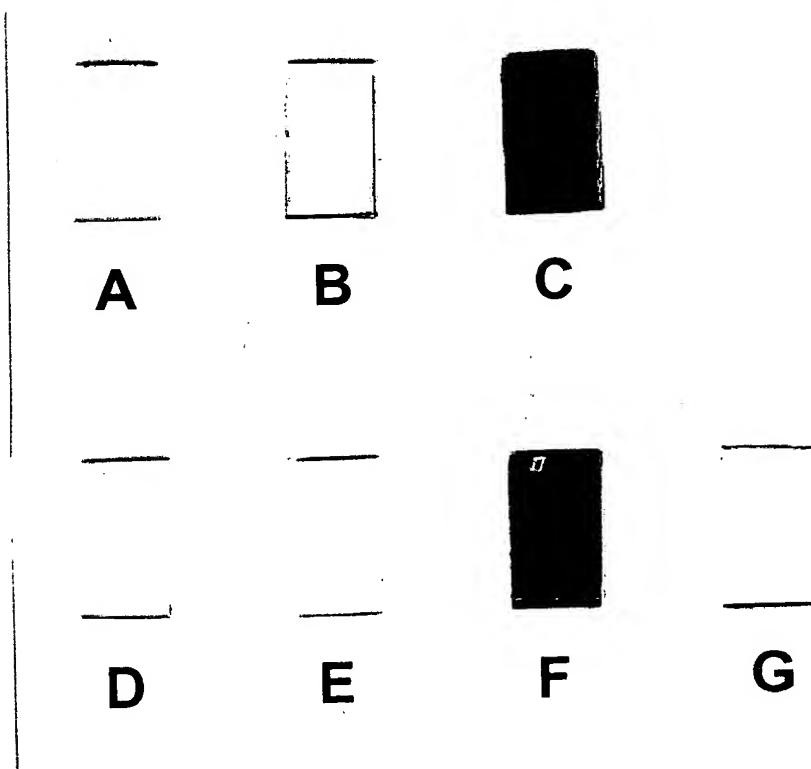
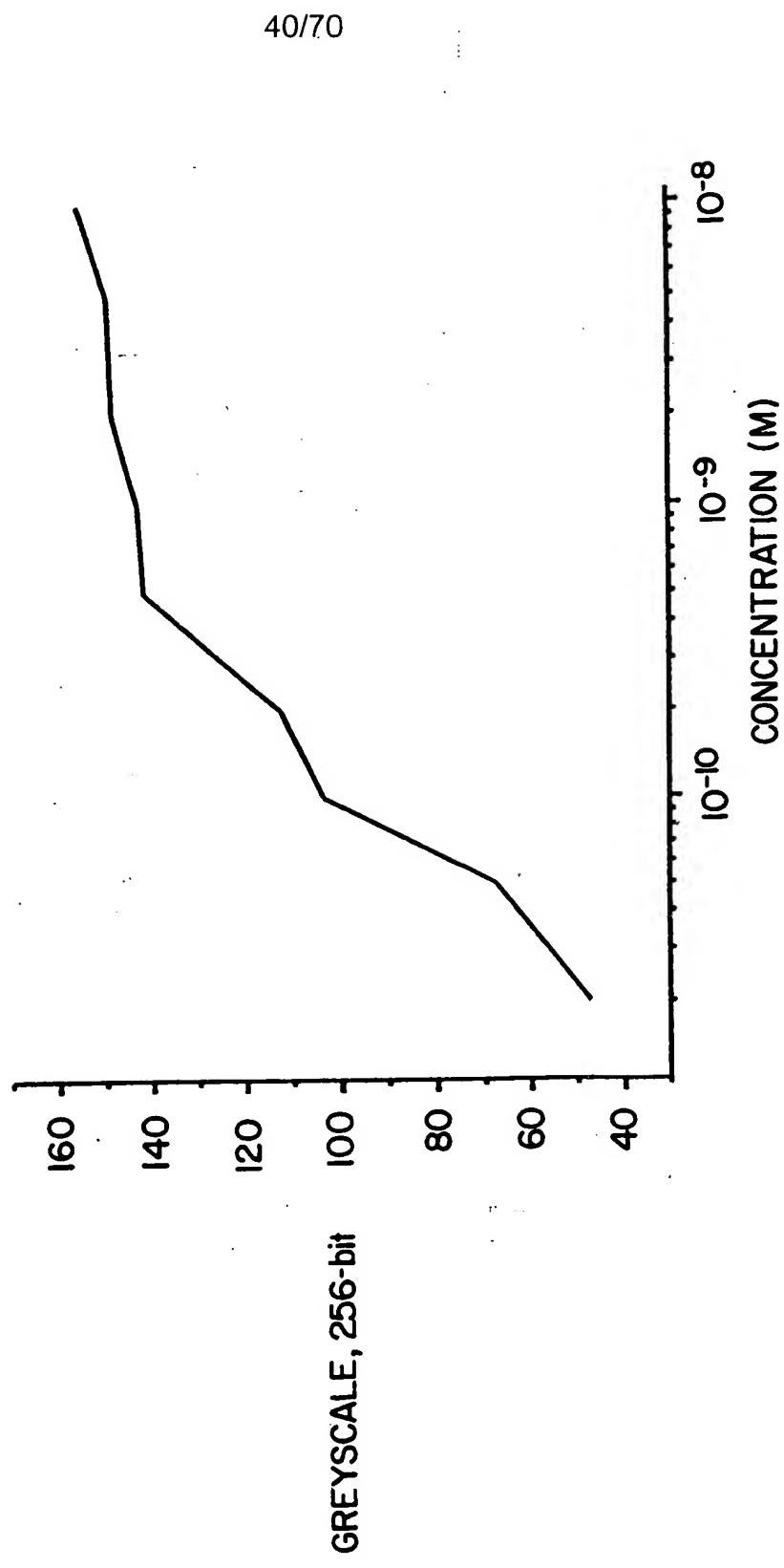


FIG. 34



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FIG.35A

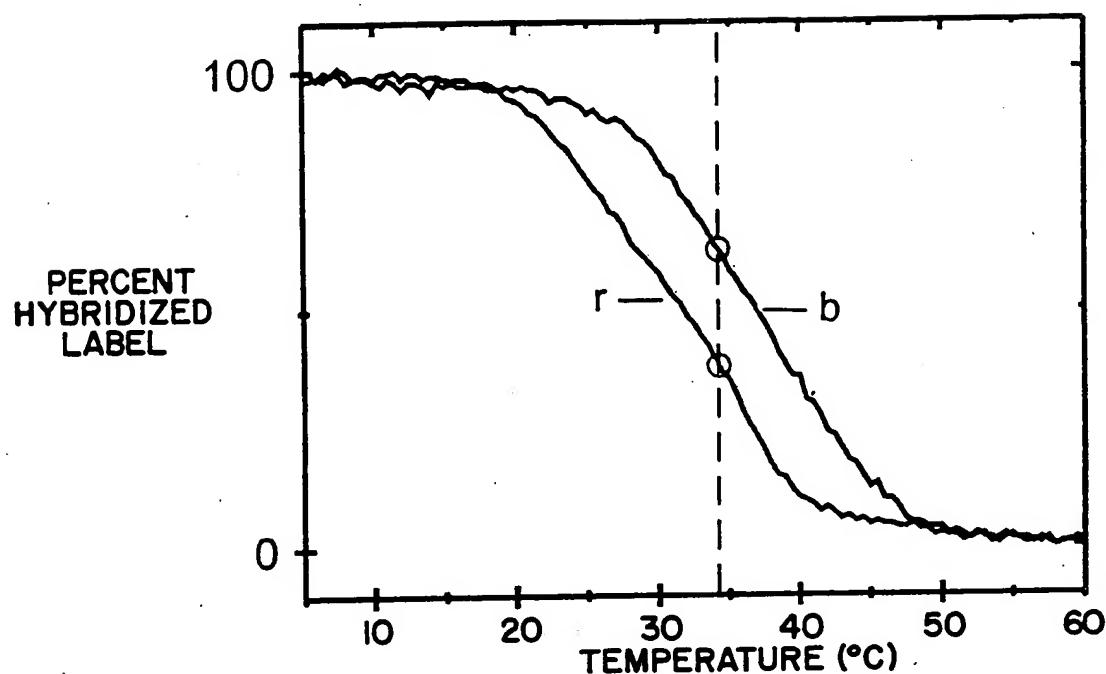
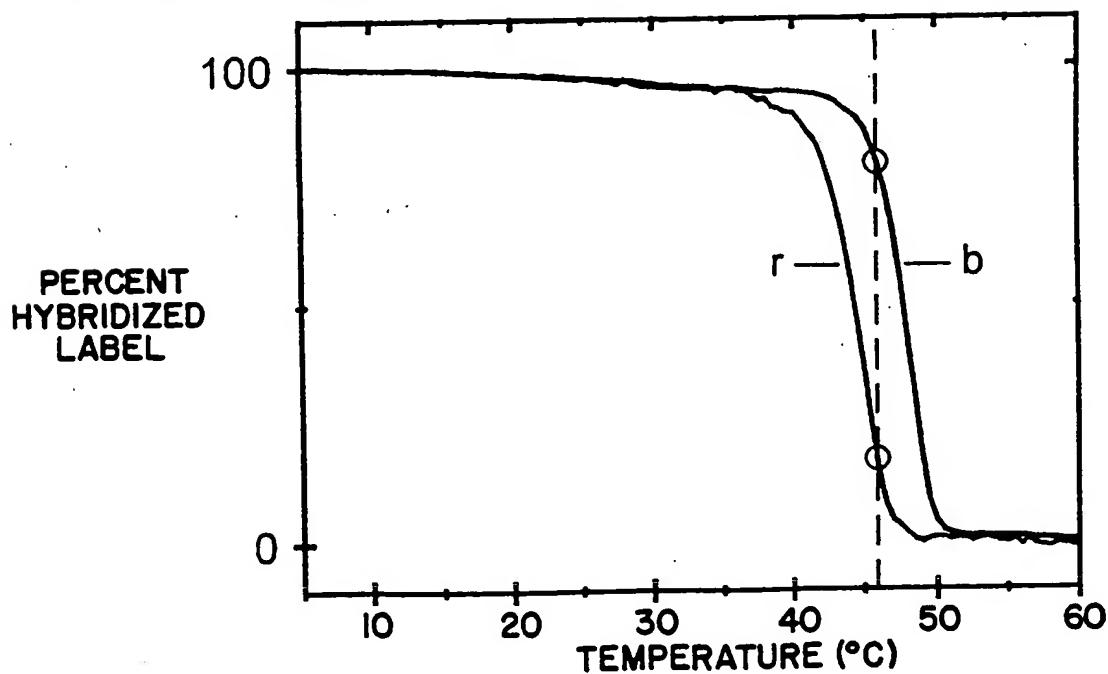


FIG.35B



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FIG. 36A

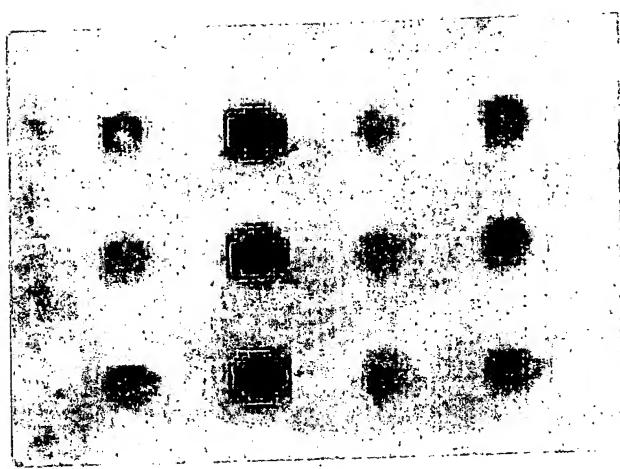
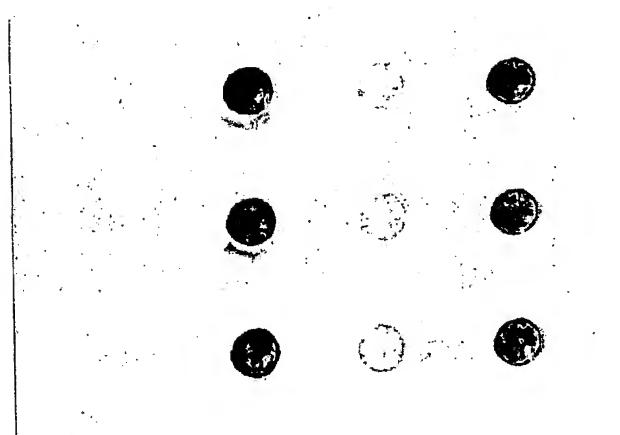


FIG. 36B



C A T G

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FIG.37A

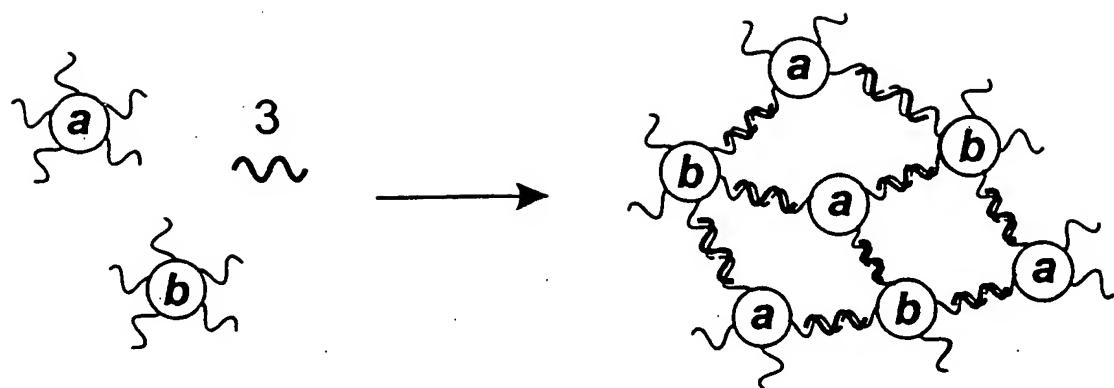


FIG.37B

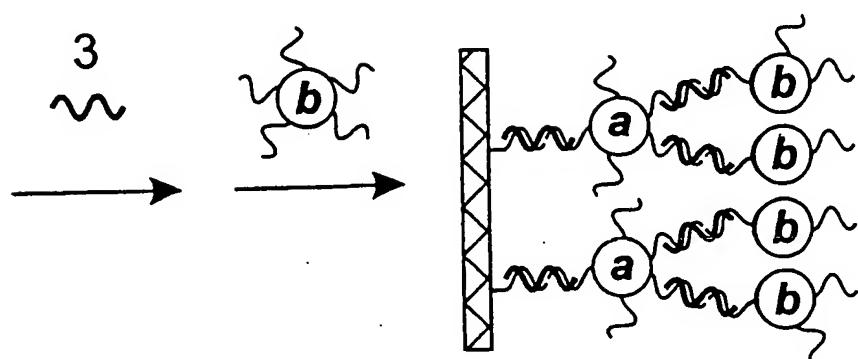
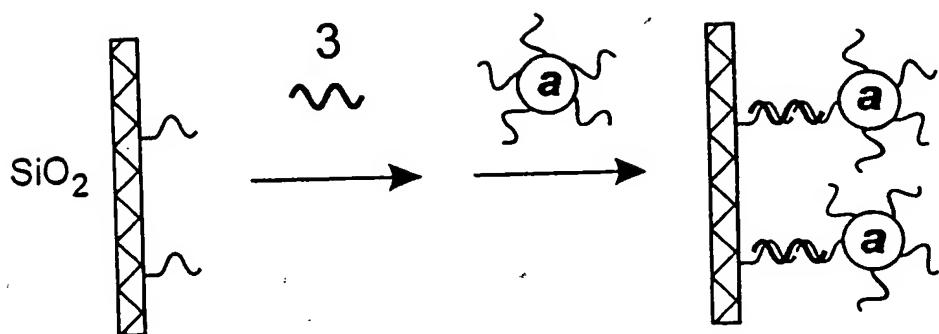


FIG.38A

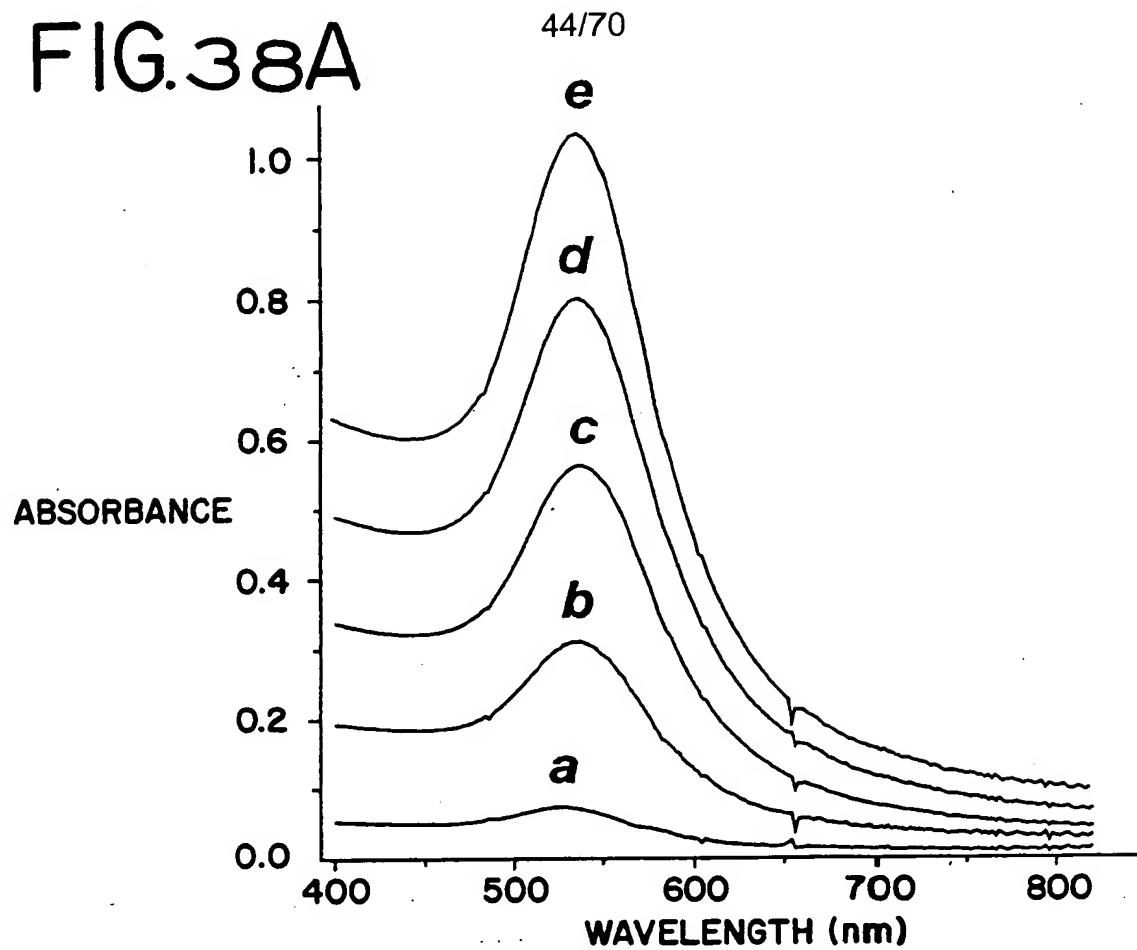
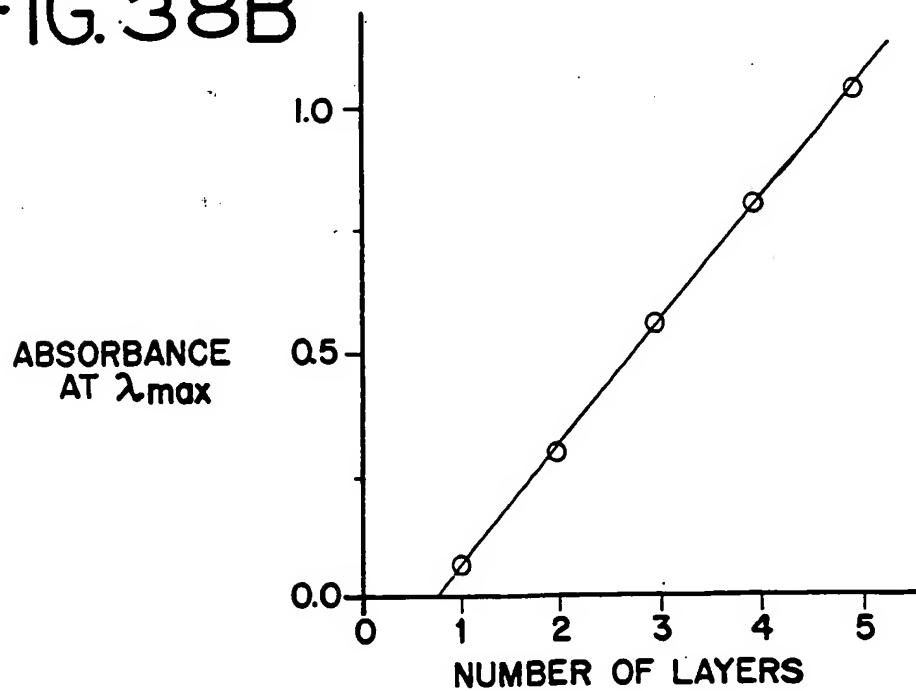


FIG.38B



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FIG. 39A

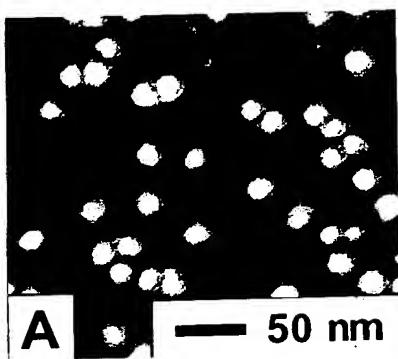


FIG. 39B

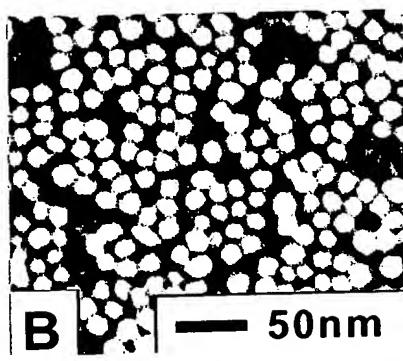


FIG.39C

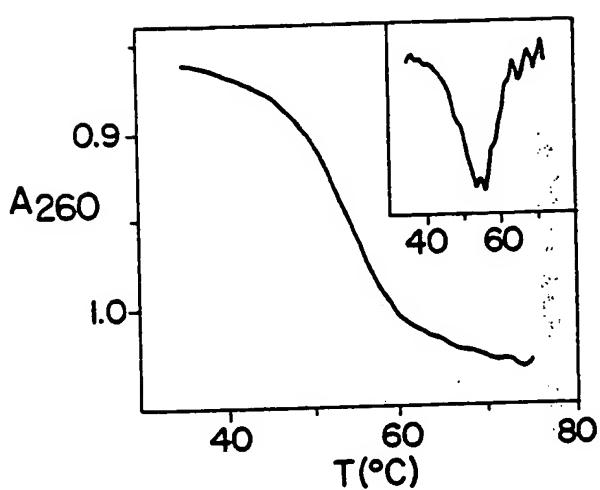


FIG.39D

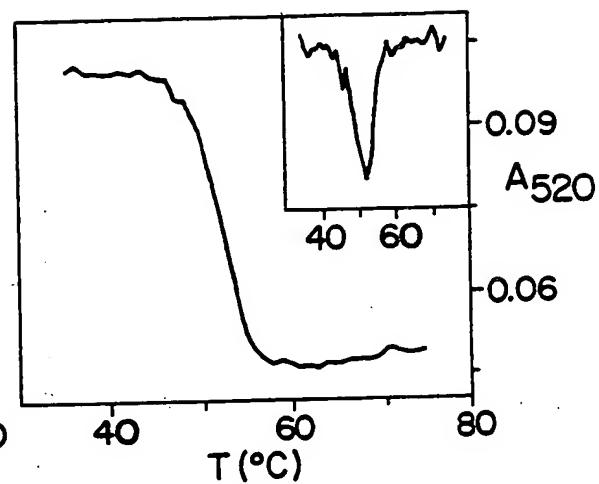


FIG.39E

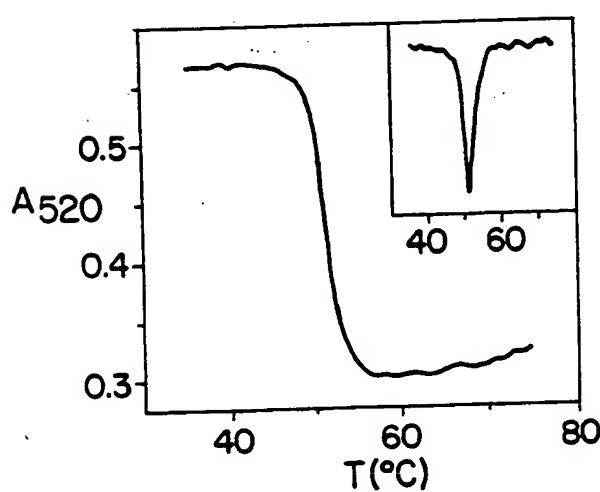
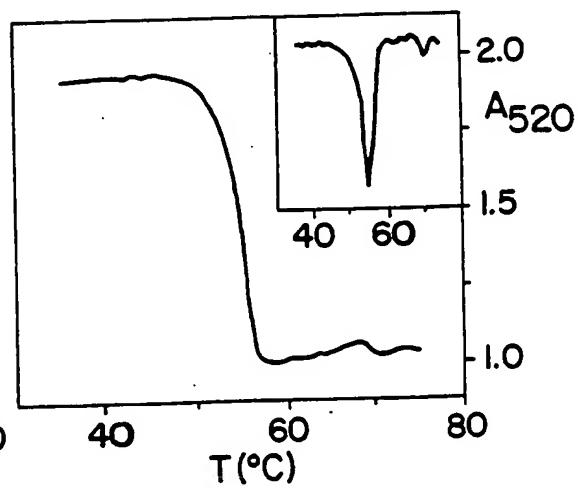


FIG.39F



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FIG. 40

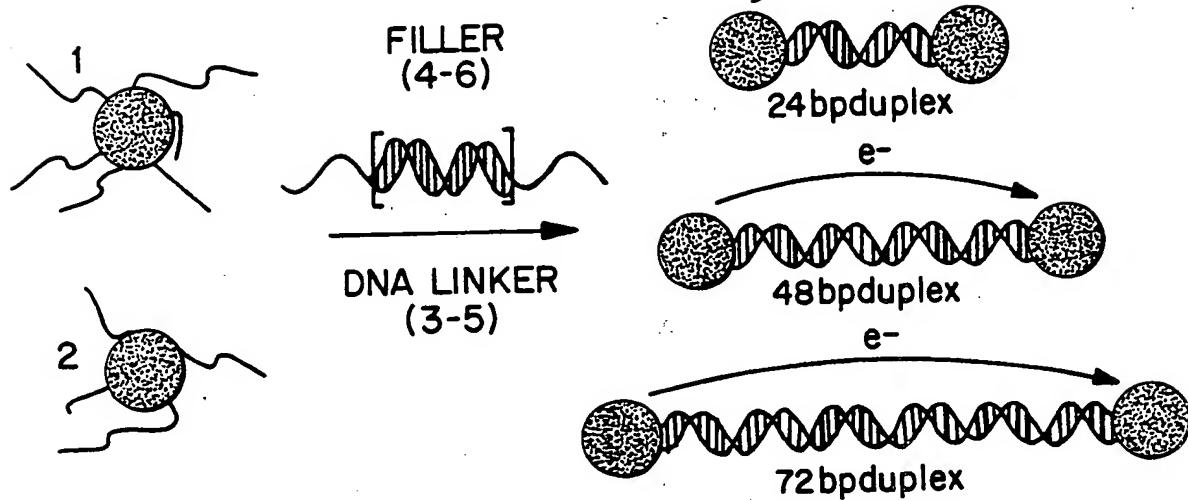


FIG. 41

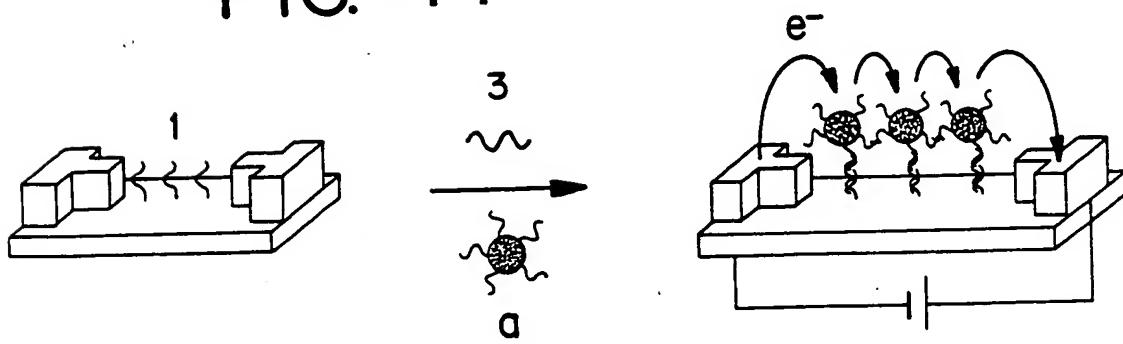
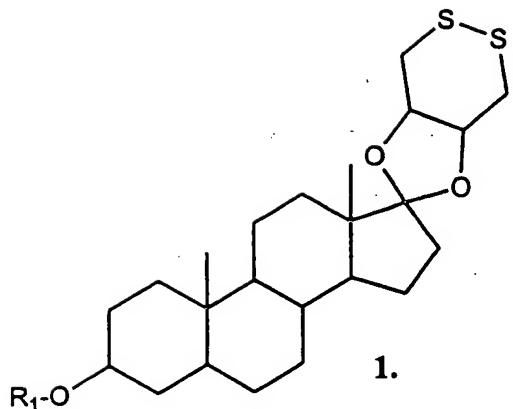


FIG. 42



II $\text{HS-(CH}_2\text{)}_6\text{OR}_1$

III $\begin{matrix} \text{S-(CH}_2\text{)}_6\text{OR}_1 \\ | \\ \text{S-(CH}_2\text{)}_6\text{OH} \end{matrix}$

R_1

a = H

b = $(\text{iPr})_2\text{NP(OCH}_2\text{CH}_2\text{CN)}$ -

c1 = 5'p(A₂₀)-TATCGTTCCATCAGCT [SEQ ID NO: 65]

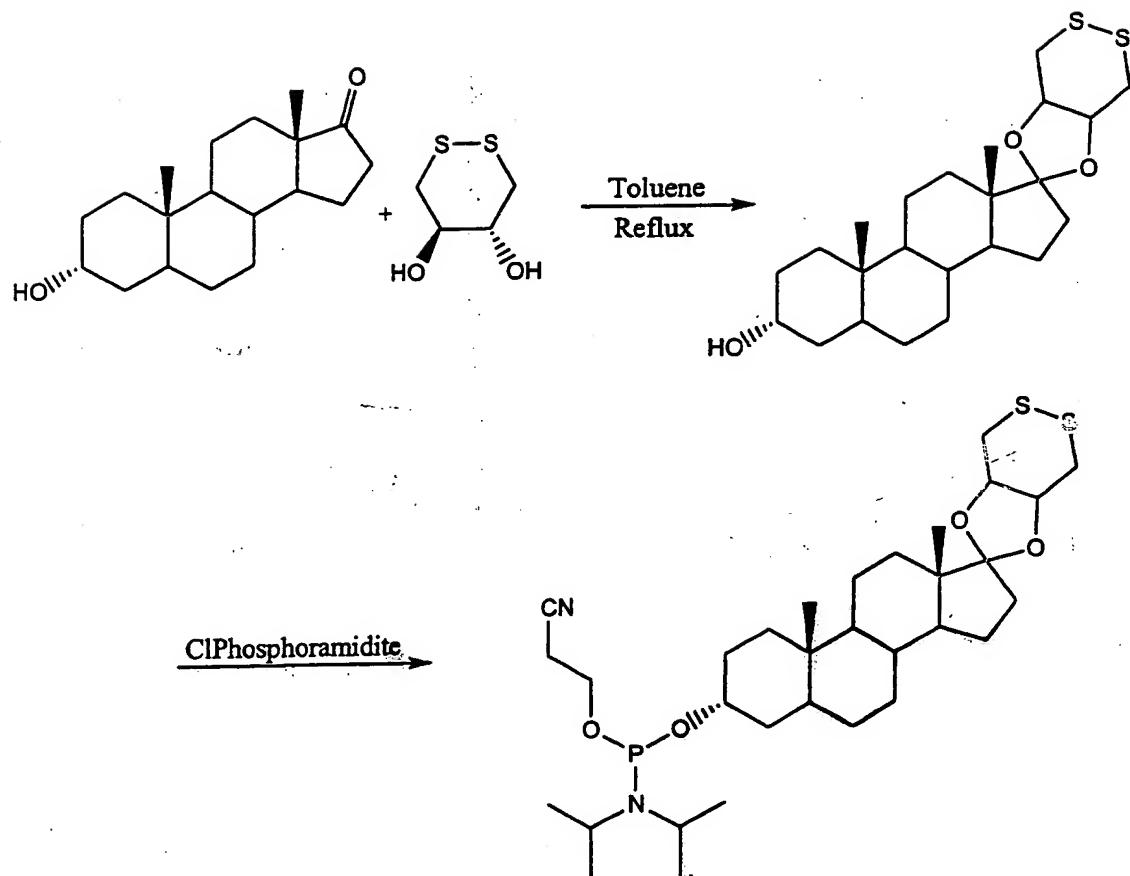
c2 = 5'-p(A₂₀)-TTGATCTTCCGTTCT [SEQ ID NO: 66]

Target I = 79-mer oligonucleotide with target region:

3'.....ATAGCAAGGTAGTCGAGCAACTAGAAAGGCAAGA.....5'
[SEQ ID NO: 67]

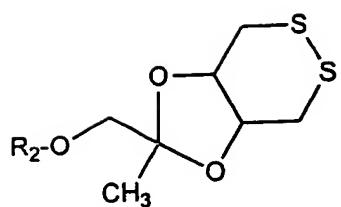
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FIG. 43



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FIG. 44



2.

R₂

a = H

b = (iPr)₂NP(OCH₂CH₂CN)-

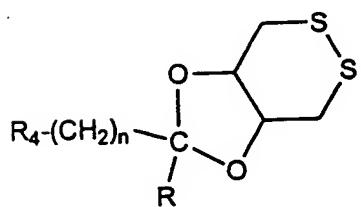
c1 = 5'-p(A₂₀)-GCAGACCTCA [SEQ ID NO: 68]

c2 = 5'-p(A₂₀)-CCTATGTGTCG [SEQ ID NO: 69]

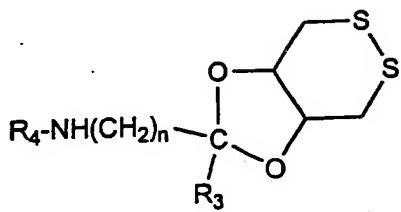
D = 5'-p(A₂₀) [SEQ ID NO: 70]

Target I = 63-mer oligonucleotide with target region:

3'-.....CGTCTGGAGTGGATAACACAGC.....5'
[SEQ ID NO: 71]



3.



4.

R₃ = hydrogen, an alkyl group, an aryl group, or a substituted alkyl or aryl group

R₄ = an attached oligonucleotide or modified oligonucleotide

FIG. 45

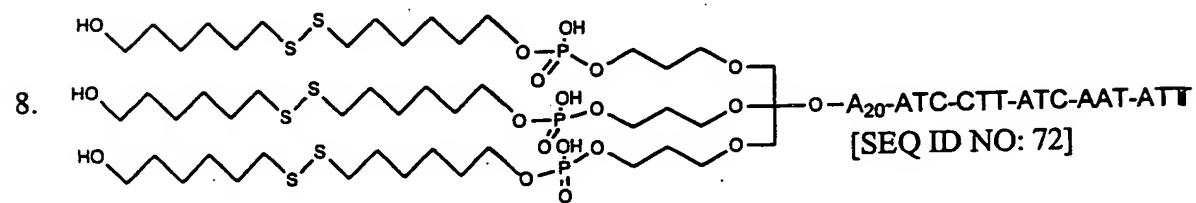
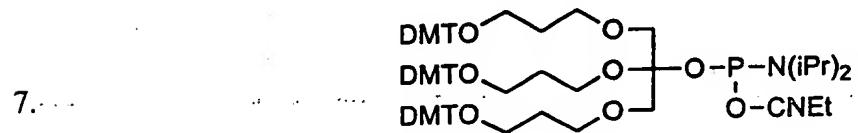
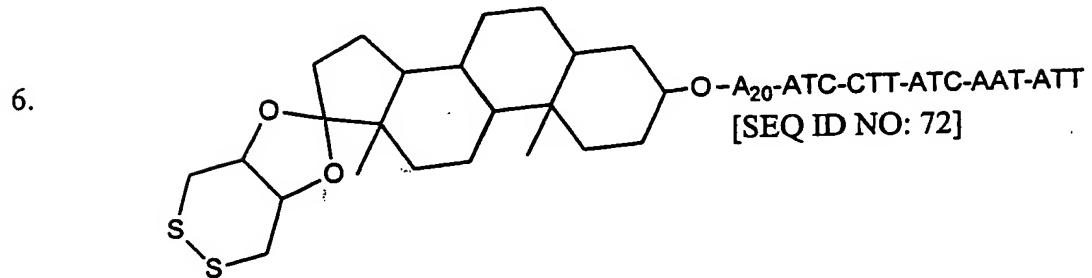
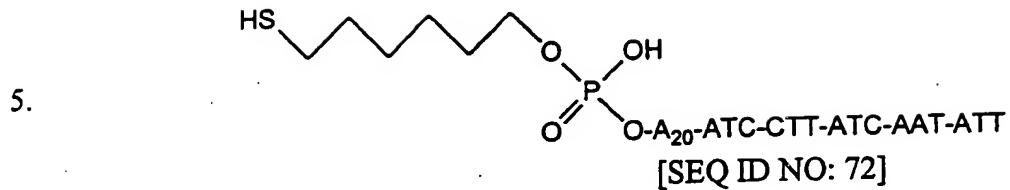
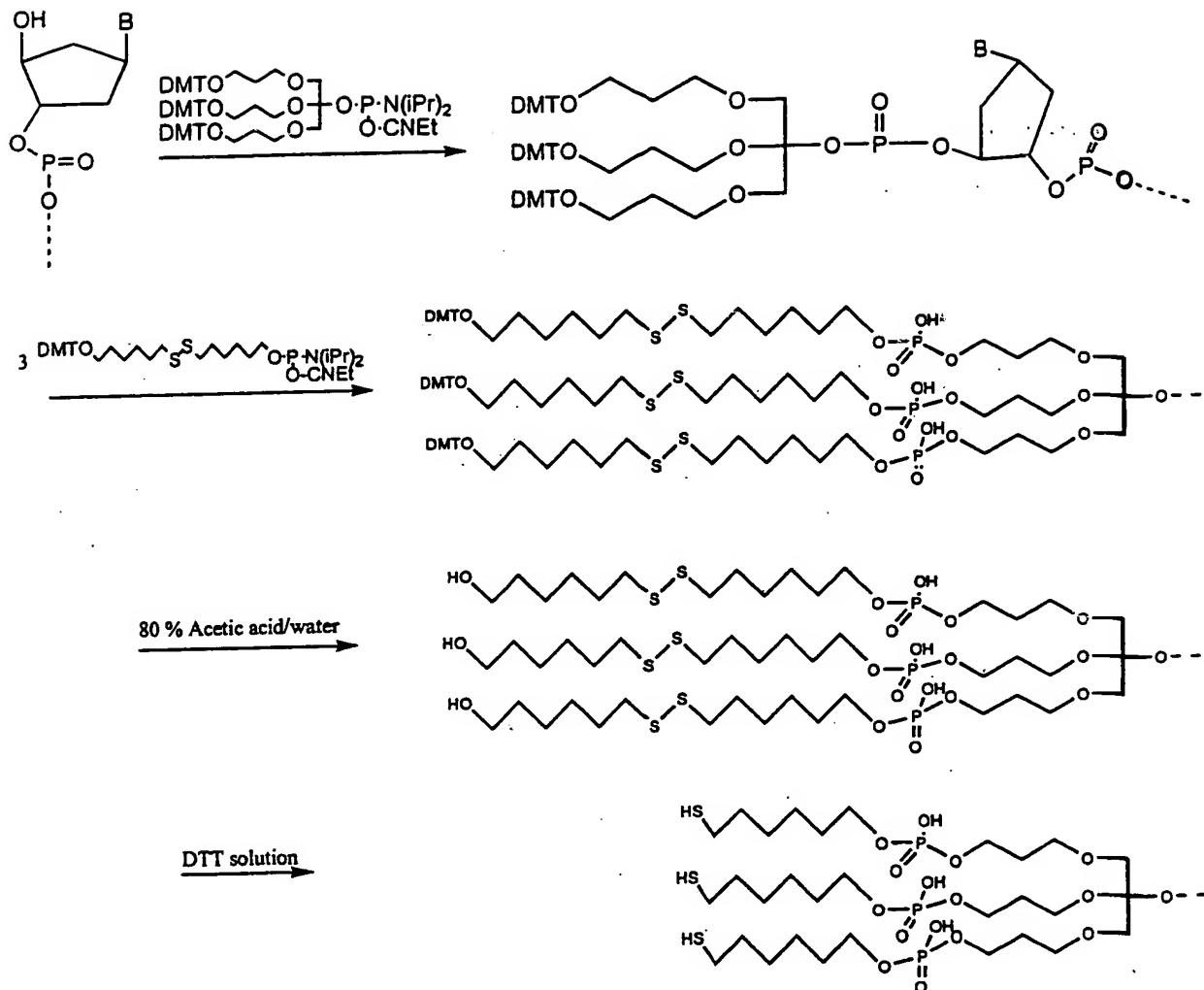


FIG. 46



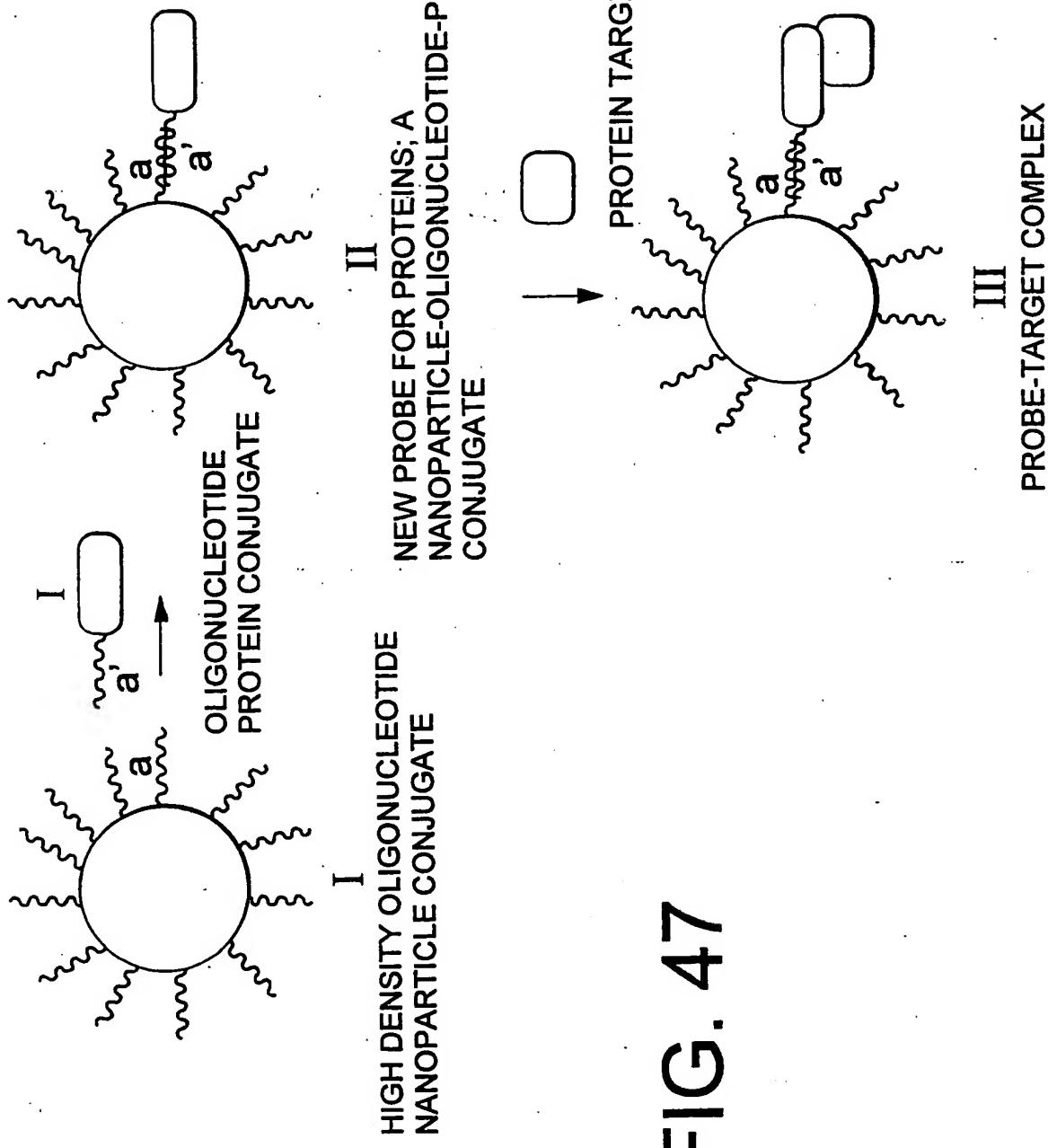
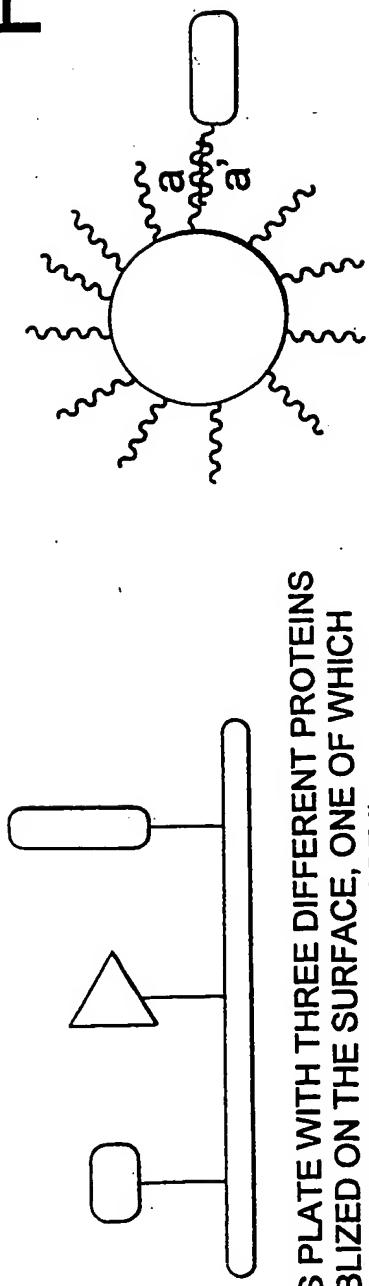


FIG. 48

GLASS PLATE WITH THREE DIFFERENT PROTEINS
IMMOBILIZED ON THE SURFACE, ONE OF WHICH
BINDS TO THE PROTEIN IN PROBE II

II

NEW PROBE FOR PROTEINS; A
NANOPARTICLE-OLIGONUCLEOTIDE-PROTEIN
CONJUGATE

1. EXPOSE PLATE TO THE PROBE SOLUTION
2. WASH AWAY UNBOUND NANOPARTICLE PROBE
3. OBSERVE PRESENCE OF BOUND NANOPARTICLES AT
SITE OCCUPIED BY THE FIRST PROTEIN IN THE SERIES.

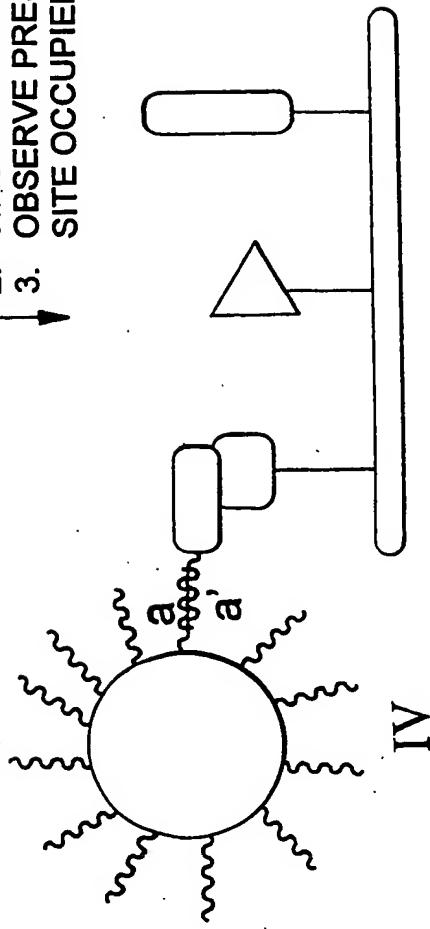
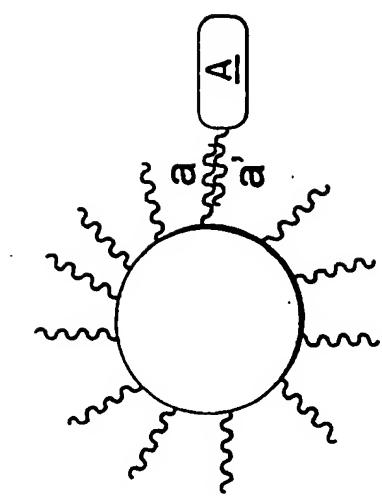
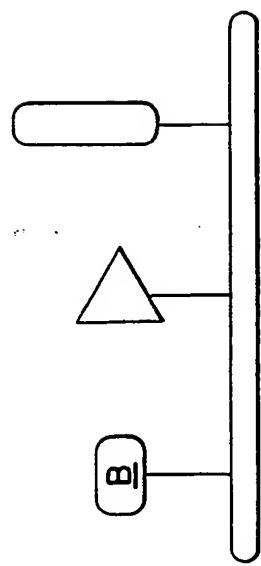
**IV**

FIG. 49



II'
NANOPARTICLE-OLIGONUCLEOTIDE-RECEPTOR



GLASS PLATE WITH THREE DIFFERENT SUBSTANCES
IMMOBILIZED ON THE SURFACE, ONE OF WHICH (B)
BINDS TO THE RECEPTOR UNIT (A) IN II'.

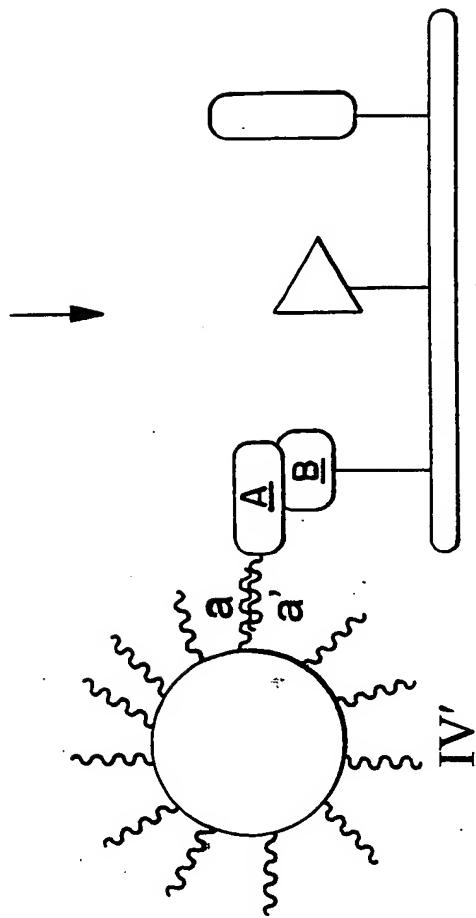


FIG. 50A

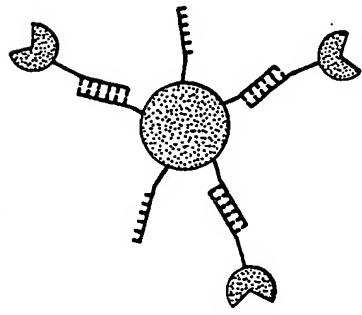
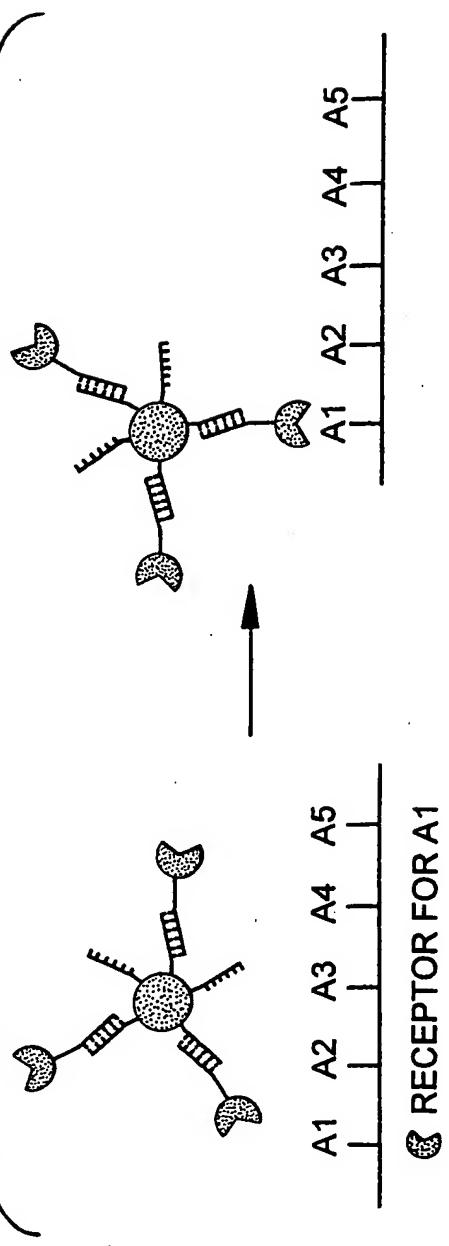


FIG. 51A



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FIG. 50B

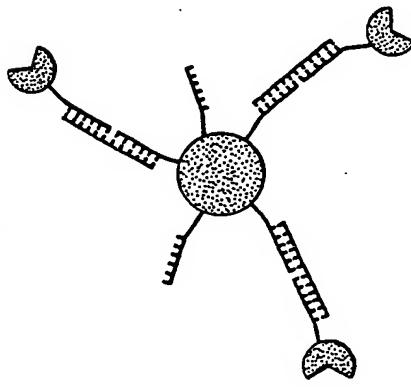
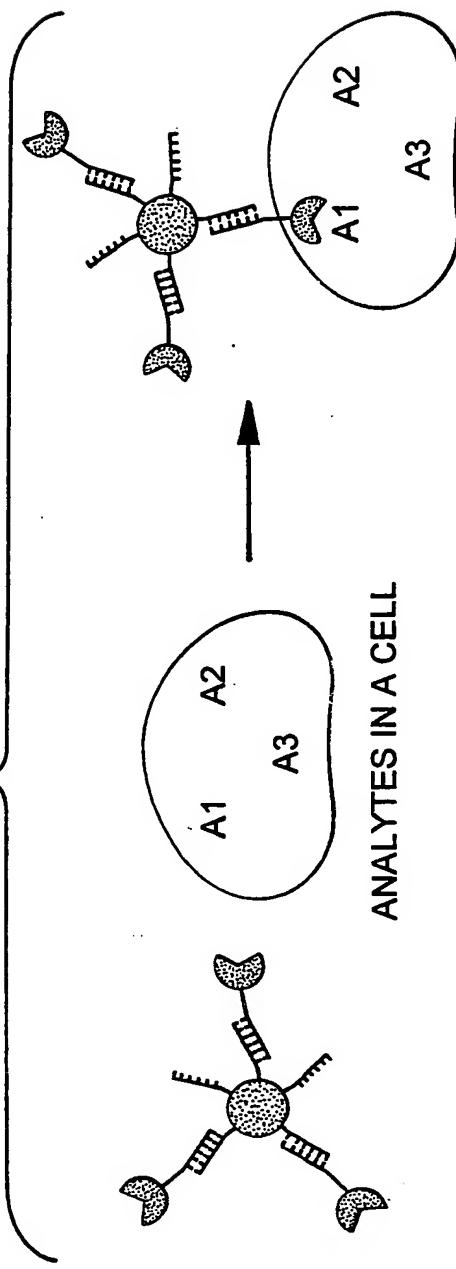


FIG. 51B



ANALYTES IN A CELL

FIG. 52A

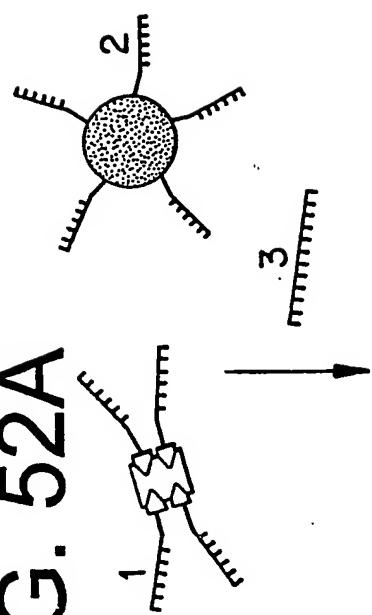
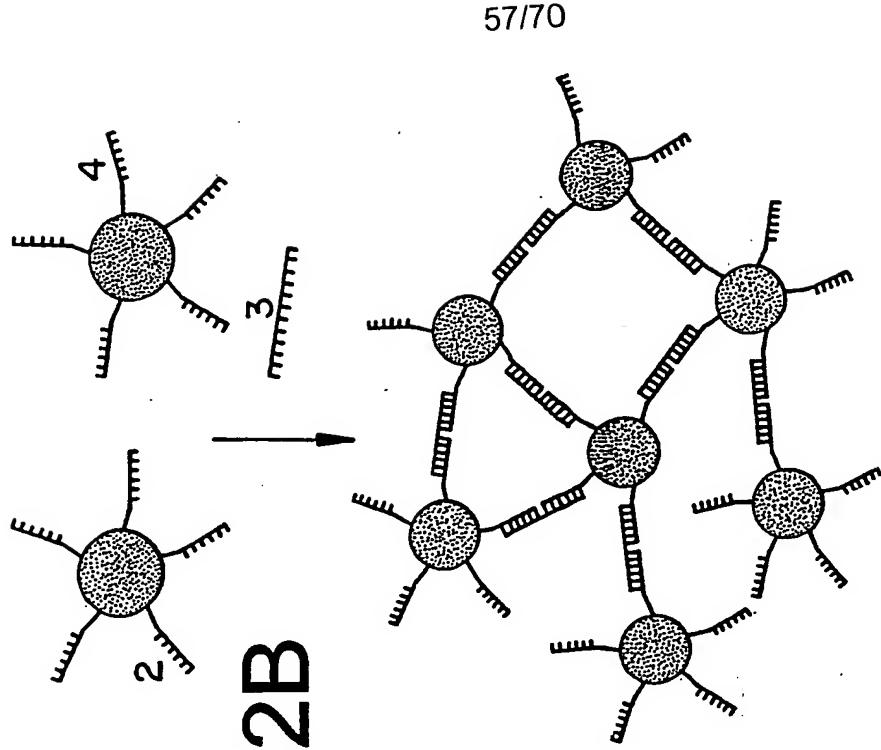


FIG. 52B



- 1 3' biotin-TEG-A₁₀-ATG CTC AAC TCT 5' [SEQ. ID NO. 73]
2 5' SH(CH₂)₆-A₁₀-CGC ATT CAG GAT 3'
3 5' TAC GAG TTG AGA ATC CTG AAT GCG 3' [SEQ. ID NO. 74]
4 3' SH(CH₂)₃-A₁₀-ATG CTC AAC TCT 5' [SEQ. ID NO. 75]

● 13 nm Au NANOPARTICLES [] STREPTAVIDIN

● 13 nm Au NANOPARTICLES

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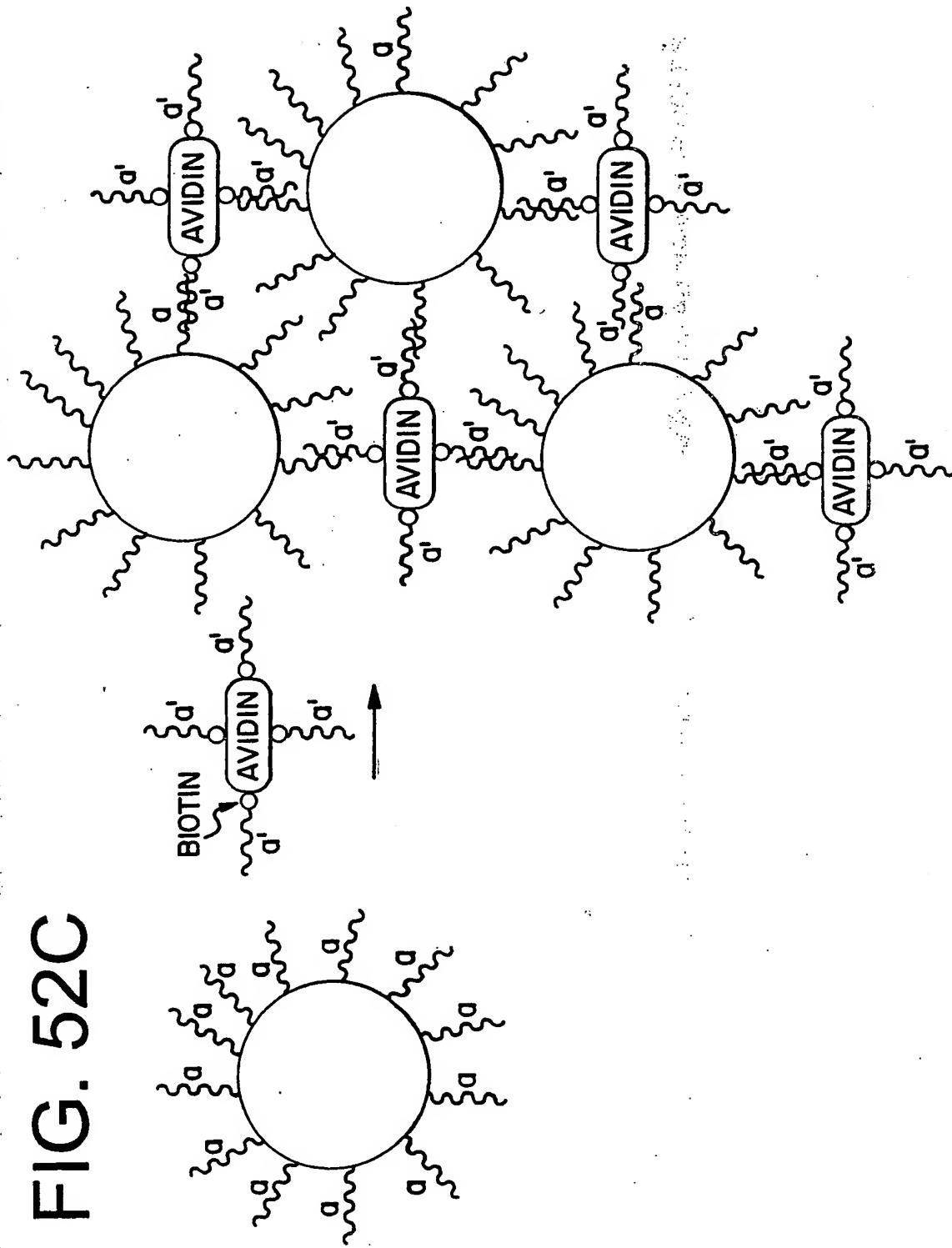


FIG. 52C

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FIG. 53

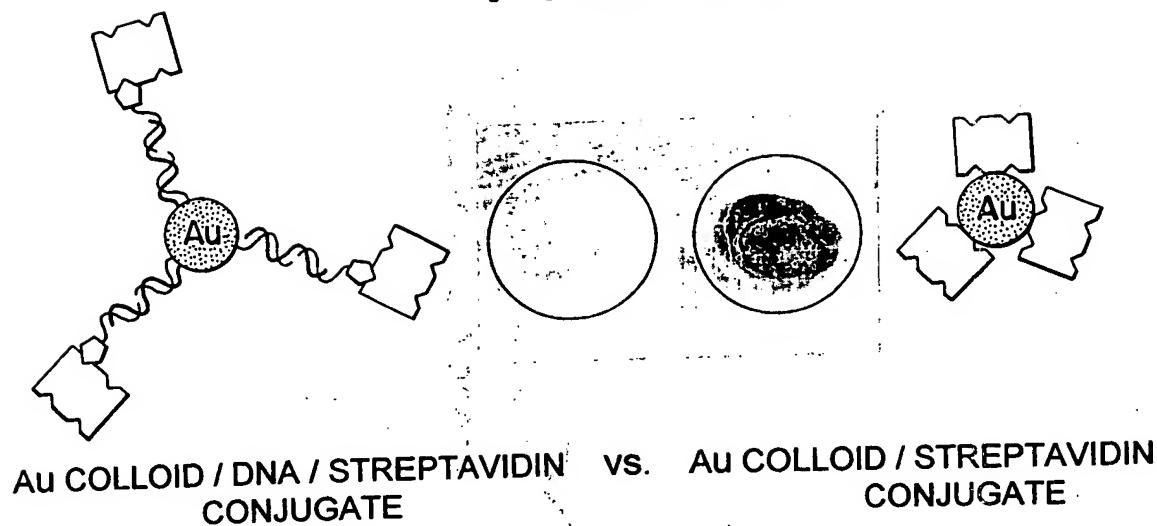


FIG. 54

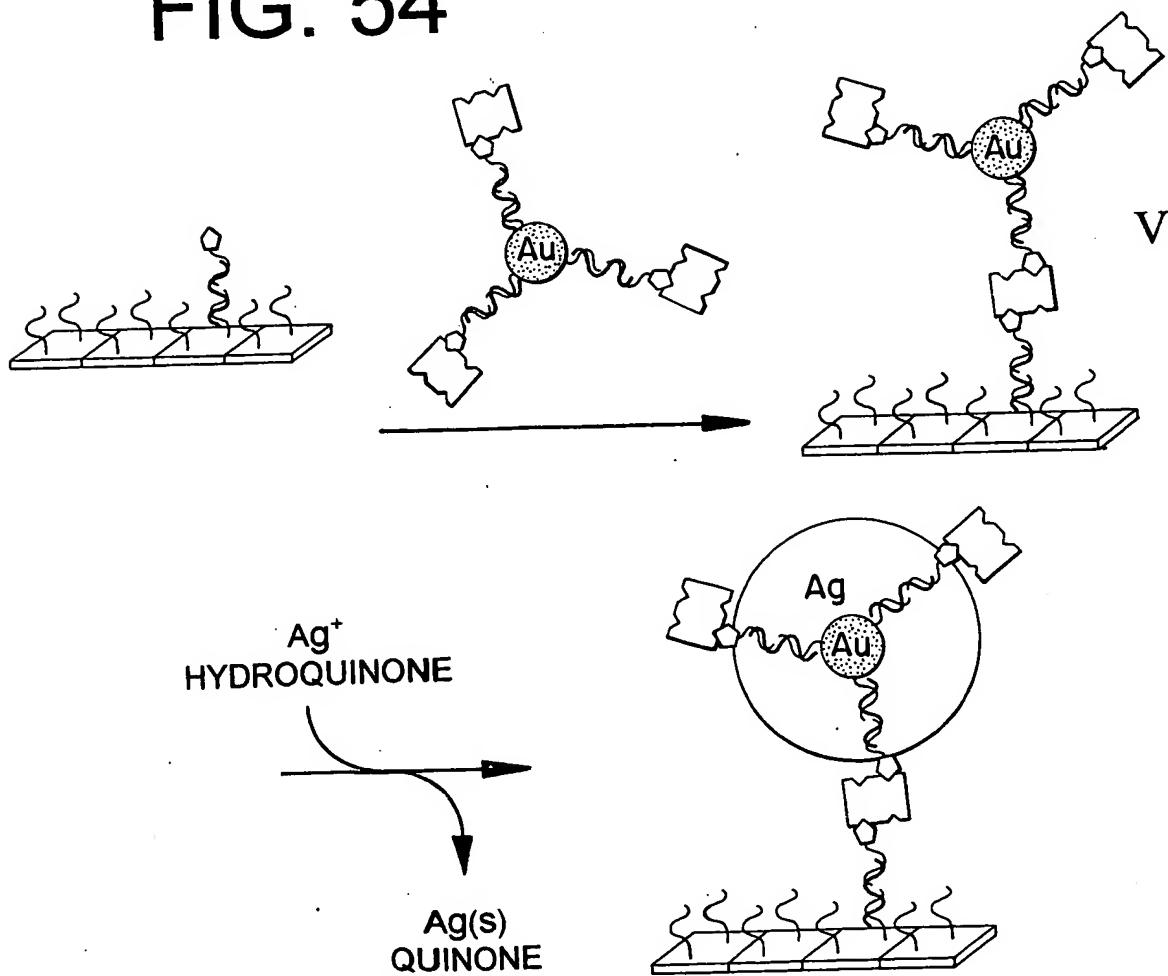


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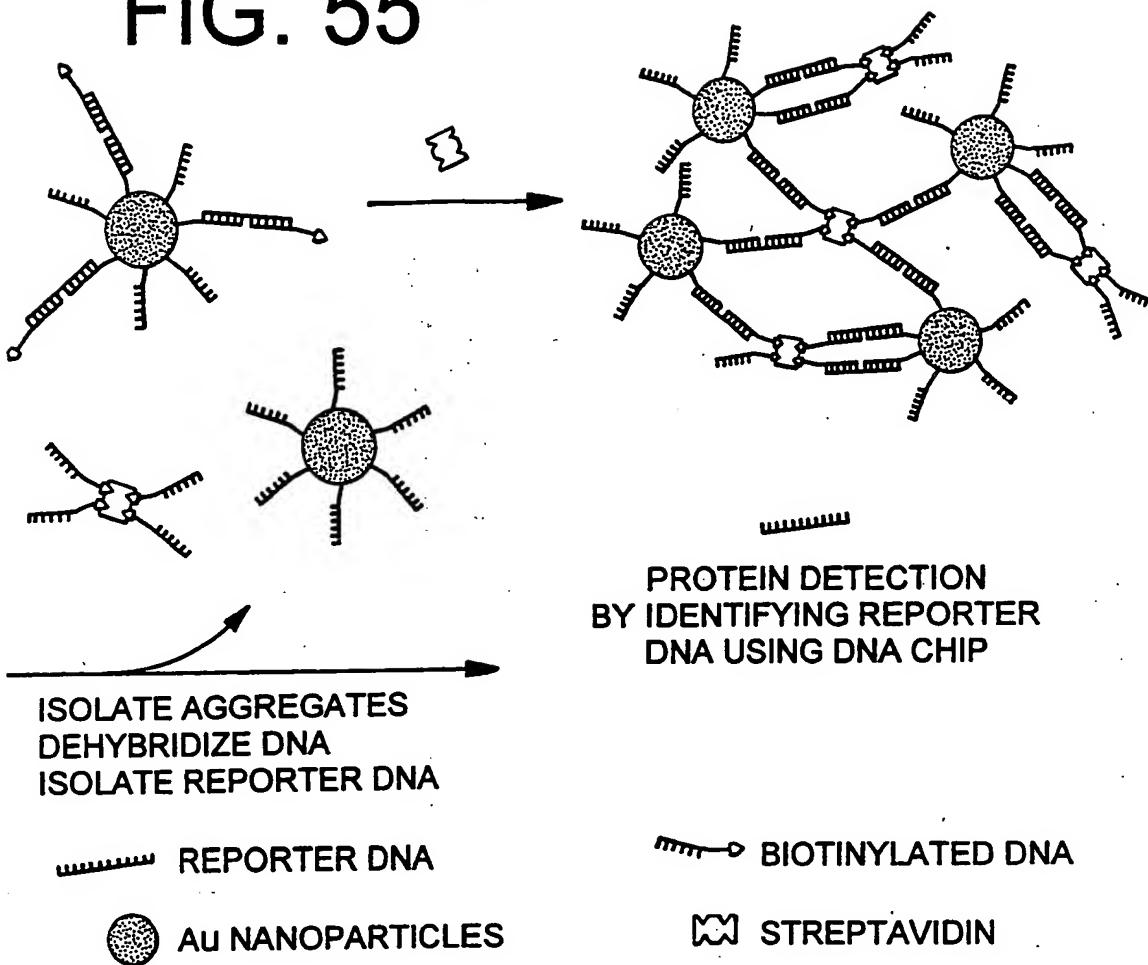
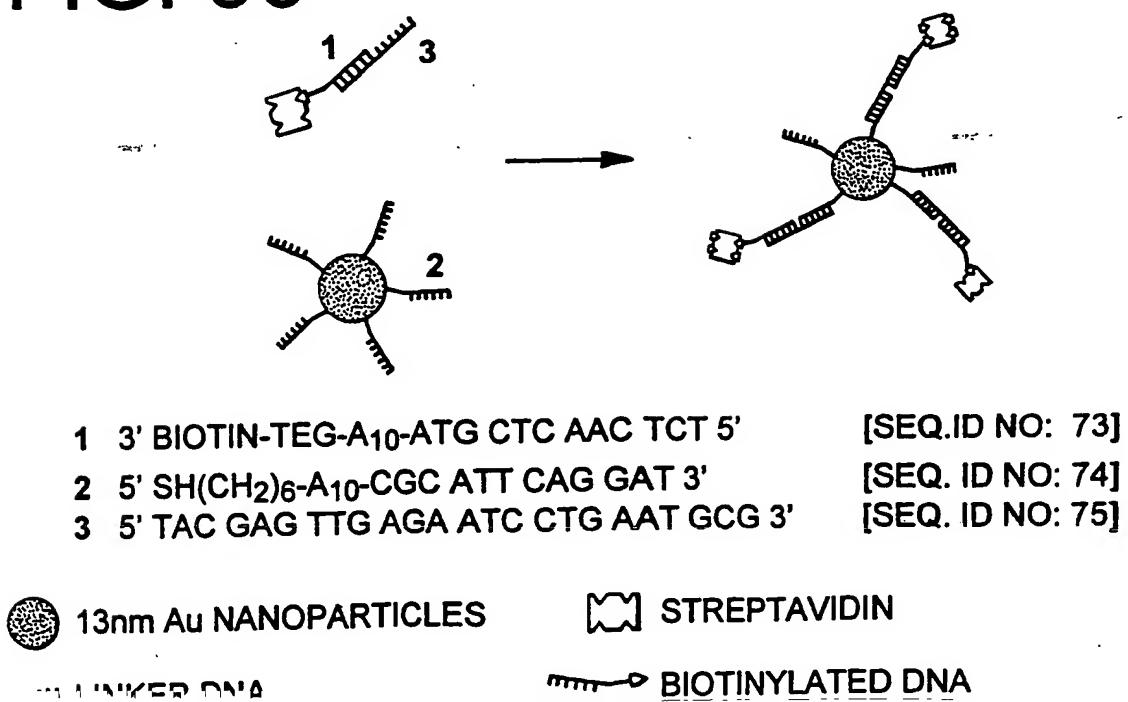


FIG. 56



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FIG.57A

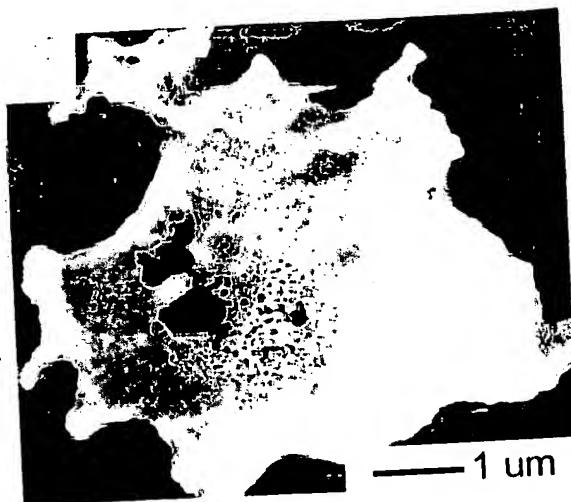
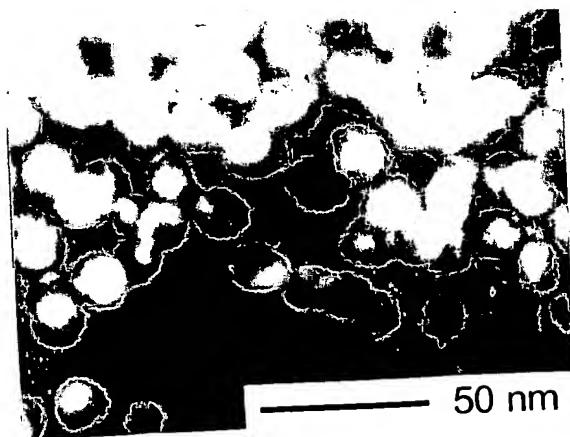


FIG.57B



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FIG. 58A

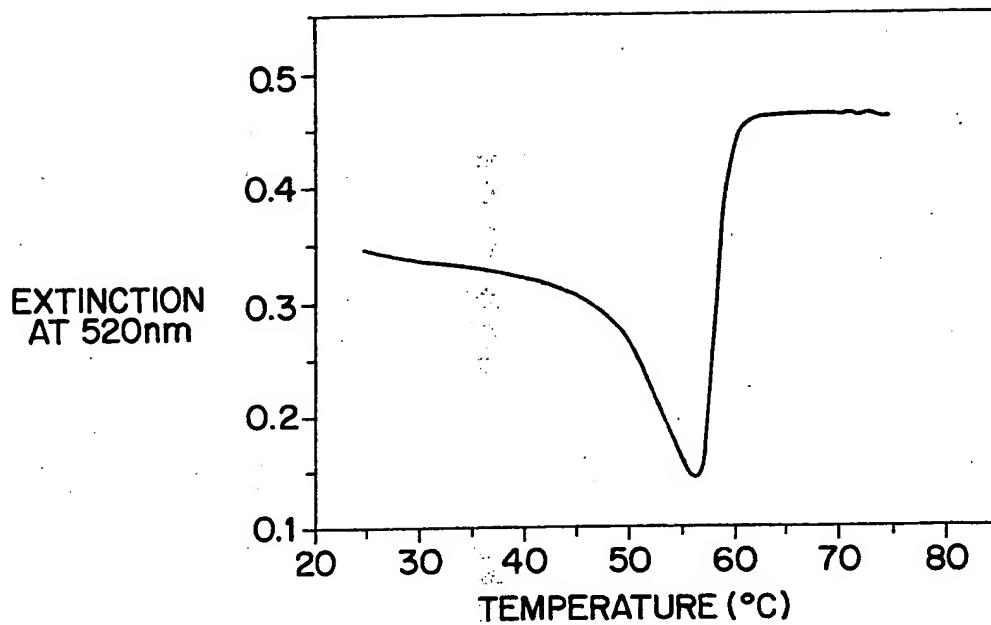


FIG. 58B

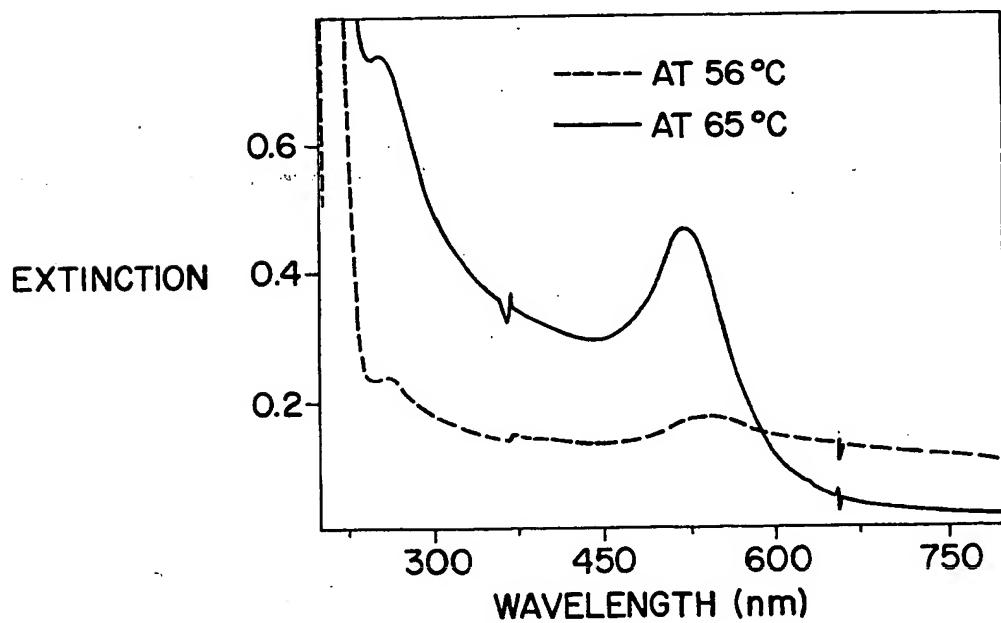
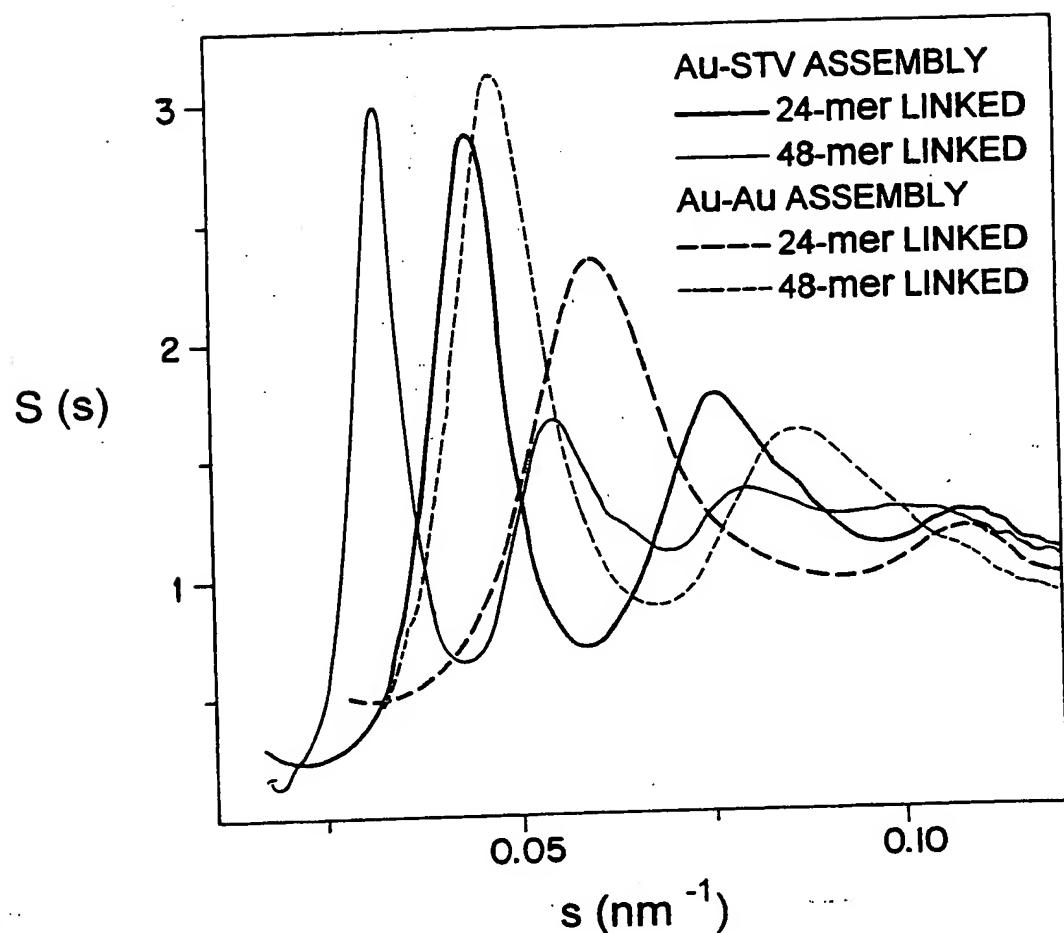


FIG. 59

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FIG. 60

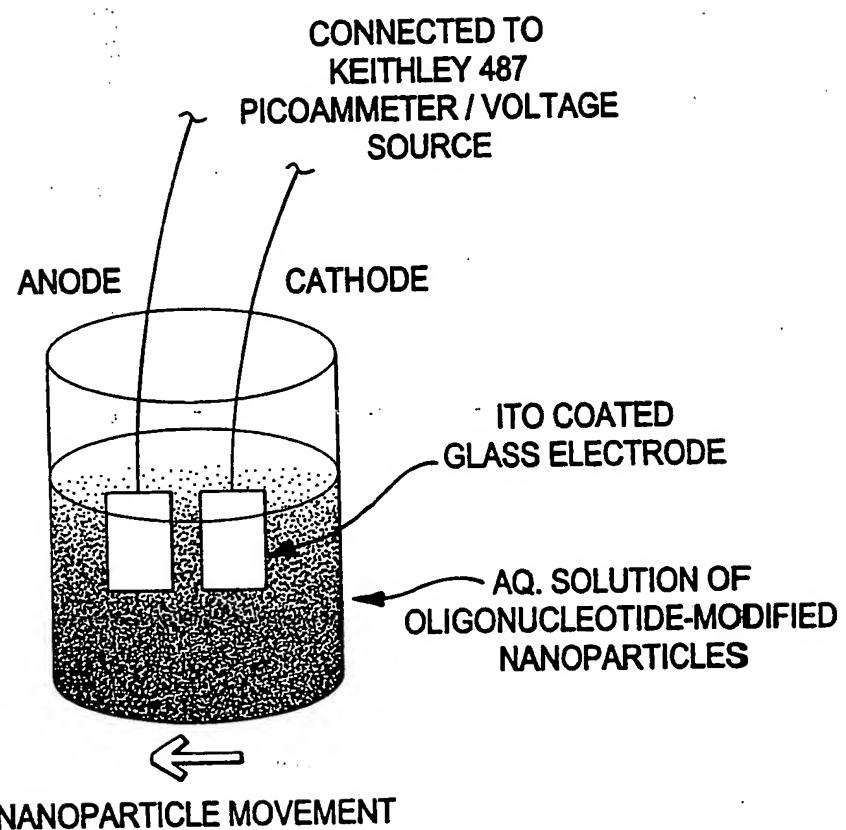
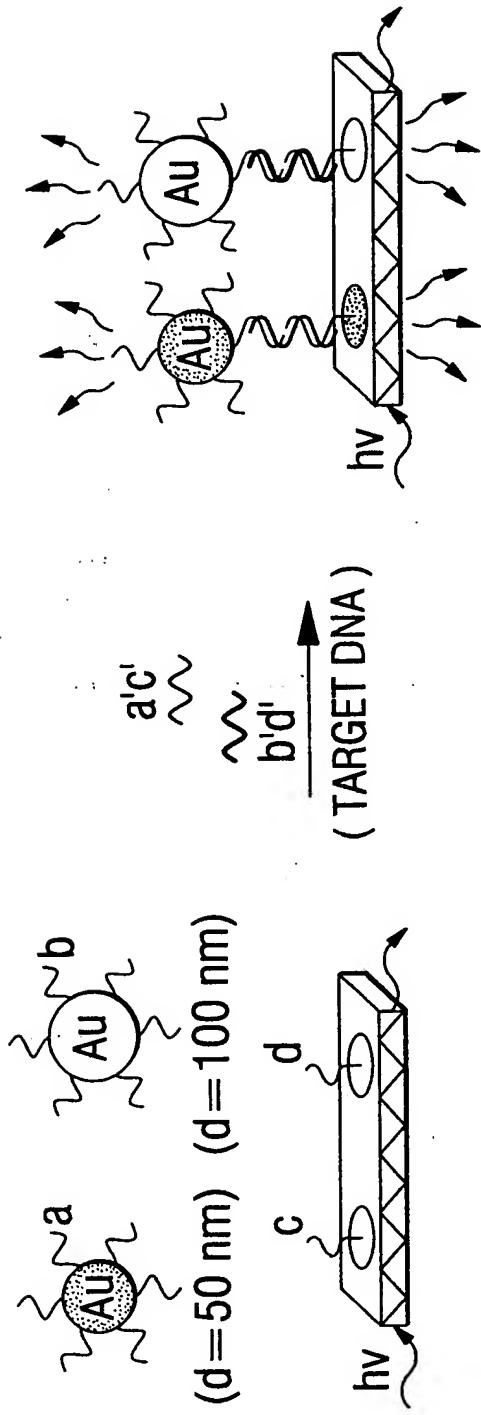


FIG. 61A



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FIG. 61B

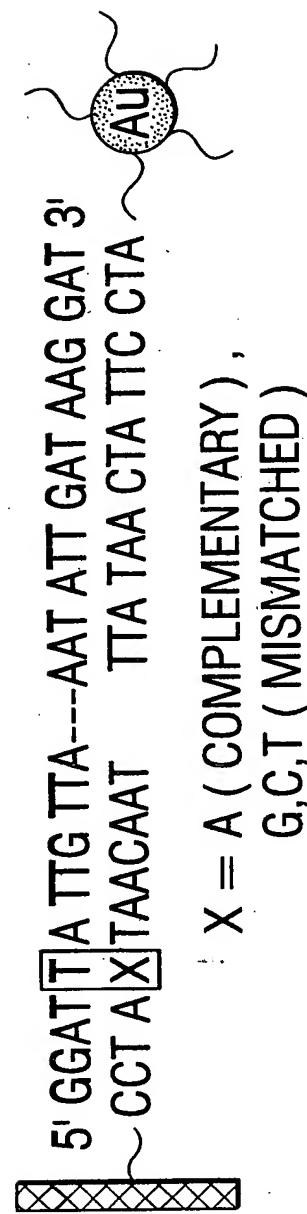


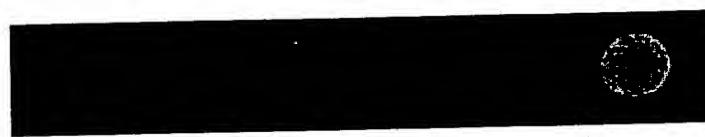
FIG. 62

Test for Target
Sequence *a'c'*

A



B



C



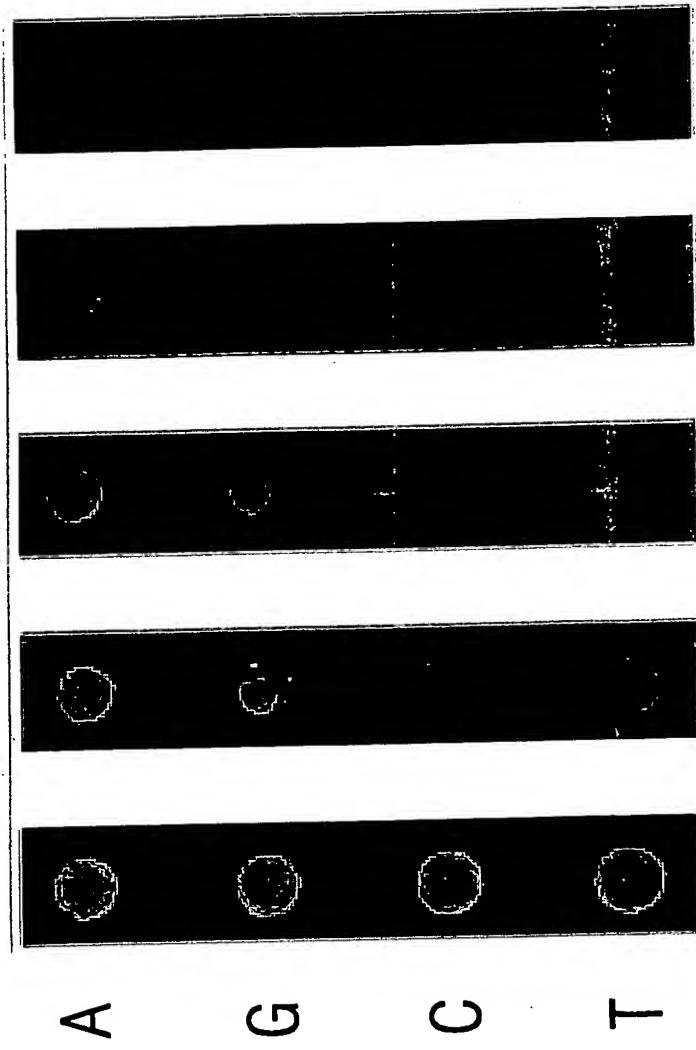
D



Test for Target
Sequence *b'd'*

FIG. 63A

25 °C 49 °C 52 °C 55 °C 59 °C



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FIG. 63B

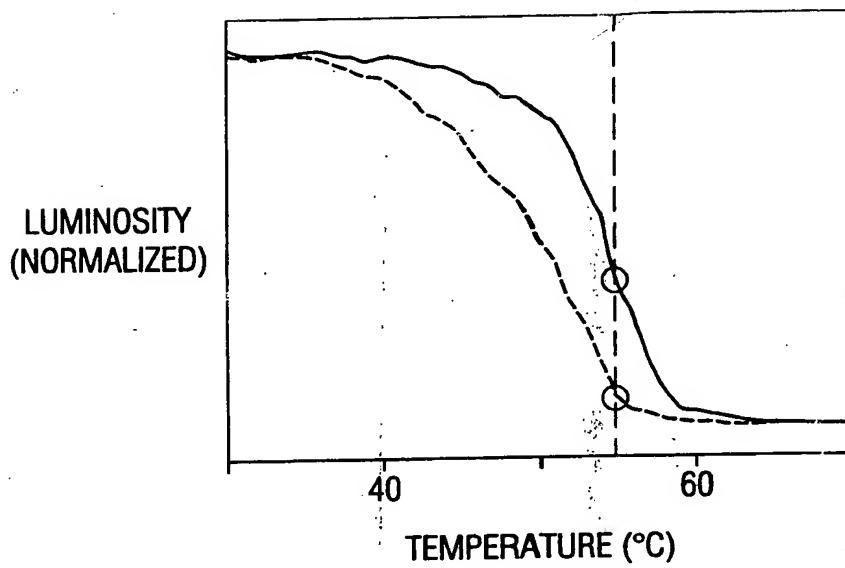
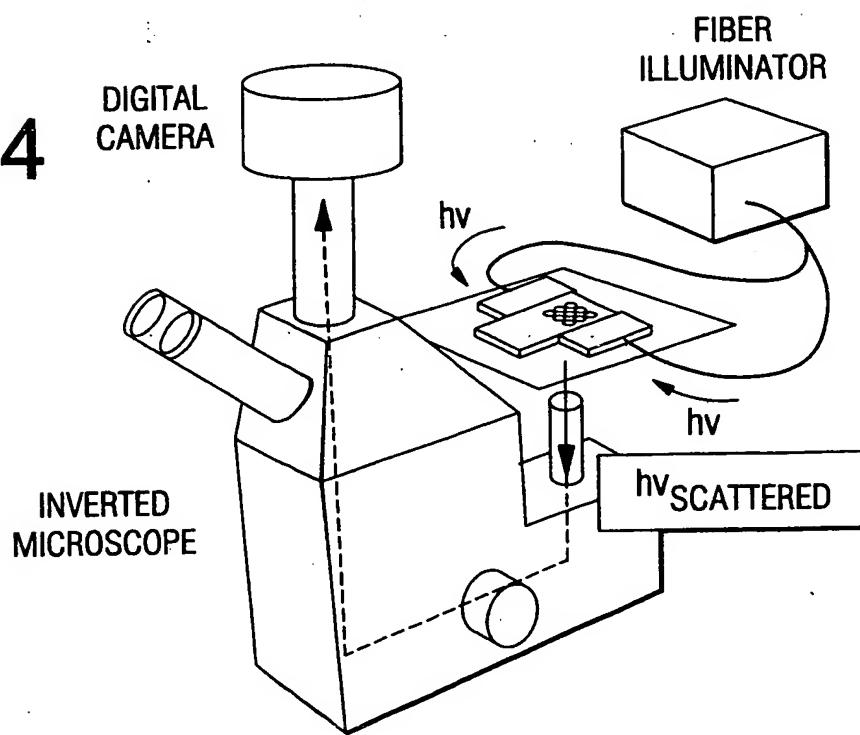


FIG. 64



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FIG. 65A

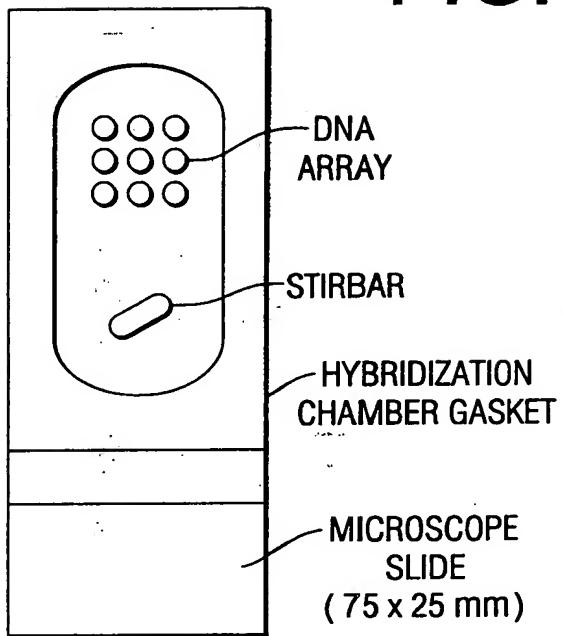
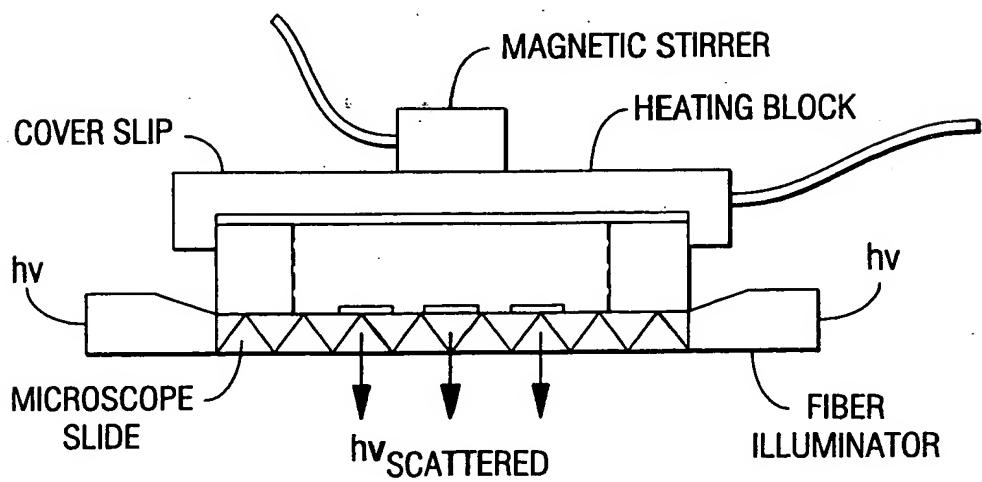


FIG. 65B



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FIG. 66

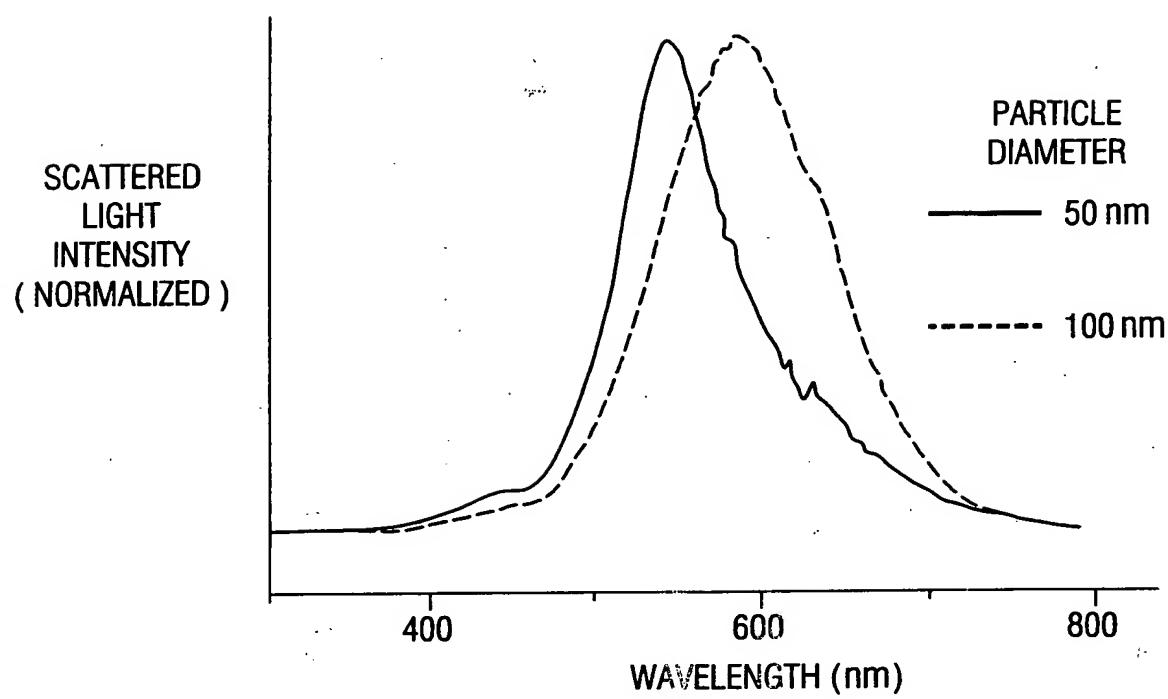


FIG. 67

